National Rabies Symposium (1966: National Communicable Disease Center)

PROCEEDINGS

NATIONAL RABIES SYMPOSIUM

National Communicable Disease Center
Atlanta, Georgia

MAY 5-6, 1966

Co-sponsors: *AVMA Council on Public Health and Regulatory Veterinary Medicine*
Veterinary Public Health Section, Epidemiology Program, CDC

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
Bureau of Disease Prevention and Environmental Control
National Communicable Disease Center
Atlanta, Georgia 30333

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Purposes and Objectives of the Symposium

Don H. Spangler, D.V.M.[1]

It is a great honor and pleasure for me to bring you greetings from the American Veterinary Medical Association and to wish you every success for your deliberations and for the actions that are certain to result from this National Rabies Symposium.

The veterinary profession is quite aware of the great significance of this meeting. Rabies is one of the oldest, one of the most dangerous, and one of the most stubborn plagues of both man and animal. Fortunately, in this country the veterinary profession, working hand in hand with other health professions and public authorities, has made rabies control impressively effective. Rabies is no longer a major threat to domesticated animals, and it has virtually disappeared as a cause of human fatalities.

Nevertheless, the very fact that this symposium is being held shows that rabies continues to worry us. Other, more qualified speakers will tell you why rabies, in spite of all our triumphs over some aspects of the disease, still looms large as a threat to this country's health, why, in fact, it is a rapidly growing threat.

My own task is to say a few words about the objective of this symposium. I don't think it was an accident that your program committee picked a veterinarian to state the objectives of this meeting. When we veterinarians are faced with a disease which is widespread, which causes considerable economic losses, which poses a grave threat to public health, and, most importantly, which we know can be successfully attacked, we historically approach it with a shocking single-mindedness. All we have to say about it is: Let's get rid of it.

We veterinarians prefer eradication to control. We always have. We believe that to live or not to live with an animals or human disease is strictly a state of mind. We believe that when we are confronted with a serious disease affecting animals, or a disease which threatens humans, no significant progress will be made in coming to terms with this disease unless positive action is taken to eradicate it.

[1]President, American Veterinary Medical Association, Chicago, Illinois.

Veterinary medicine has applied this principle repeatedly throughout its history. During the 1800's the veterinary profession, the livestock industry, and the Bureau of Animal Industry succeeded in a common effort to eradicate contagious bovine pleuropneumonia, making the United States the first of the large countries to eradicate this disease. From there we proceeded to the eradication of foot-and-mouth disease, to the eradication of vesicular exanthema, to the eradication of glanders and dourine in horses, to the eradication of the screwworm flies, of piroplasmosis, and finally of brucellosis. Today, we are embarked on a large-scale program to eradicate hog cholera.

In all of these eradication programs, certain basic principles were applied that lead to the successful culmination of the eradication program.

The first and most important principle is the conviction, the single-minded attitude, that the best protection against a disease is the eradication of the disease itself.

In addition to proper mental attitude toward disease, another principle basic to the philosophy of disease eradication is the realization that economically the establishment of eradication programs is less costly in the long run than, for example, the fire engine approach to controlling a disease once it has broken out in epidemic proportions. The research effort which contributed to the virtual eradication of cattle tick fever in this country cost approximately $65,000. That relatively small investment today saves farmers approximately $60 million a year.

Another important principle is that any successful disease eradication program requires the full understanding and cooperation of the public. When the veterinary profession and the U.S. government initiated the tuberculosis vaccination program in 1917, there was at first considerable opposition from the livestock industry. The industry feared that a program which would reveal the incidence of the disease would in some way prejudice consumers against livestock products. Veterinarians persisted in conducting their eradication programs and endeavored to educate livestock owners and the public as to the overall value of the eradication program. Slowly these efforts paid off, until the majority of livestock owners throughout the United States rendered full cooperation in working toward the eradication of tuberculosis in the United States.

Furthermore, a successful disease eradication program must be a national program. The program, to be effective, must be able to draw on the resources of national organizations equipped to direct adequate funds, research, publicity, and educational programs, and to draw into their activities state and county agencies that can implement the program at the local level.

Finally, veterinarians should not only take part in an advisory and representative capacity—they should take part in a leading capacity. It is the practicing veterinarian who has an immediate, direct, and natural relationship with all areas concerning the prevention, treatment, and cure of animal diseases. Does this relationship exclude the eradication of a disease? The record says clearly that it does not.

Have we reached, in the case of rabies, the point where we should apply both the mental attitude and the practical principles that must underlie a successful disease eradication program? I would say it might be too early to talk about the practical requirements. But I do not believe that the mental attitude which says "Let's get rid of rabies" is either premature or impractical. Rabies is on the rise. The number of animal cases occurring, which is a much more accurate measure of the disease than human deaths, is too high for comfort. Besides, one fatality per year from rabies is one fatality too many. Some years ago the American Journal of Public Health commented, "The ultimate solution to the rabies problem is predicated on the control and eventual elimination of the disease from the animal population." Several nations of the world—among them England, Australia, New Zealand, Norway, Sweden, and Denmark—have accomplished just that. Why not decide, here and now, at this symposium, to make the United States one of them? Your meeting has nothing, as far as I can see, on the program that focuses attention on the possibility of eradicating rabies. It is concerned with understanding rabies—its prevention, cure, and treatment. But shouldn't our reach be just a little higher than our grasp? I am aware of the tremendous obstacles that must be overcome before rabies eradication can become a practical reality in this country. But let us remember, during this symposium, the one great lesson of the history of disease eradication in this country: that the unwavering acceptance of the challenge of eradication leads to the discovery of facts which are needed to bring about eradication.

The purpose, then, of this symposium, as I see it, is and should be none other than to pave the way for a simple and single-minded resolution: Let's get rid of rabies.

Opening Address

W. W. Washburn, M.D. [1]

Having just come back to the States after a period of time in South Viet Nam, serving with a group of volunteer physicians in "Project Viet Nam," I might be considered to be more of a specialist in tropical medicine and the treatment of war injuries than I am in the subject of rabies.

While away we did learn one or two important things. When we first arrived in Viet Nam one of the first things we asked was how to tell the Viet Cong from the friendly Vietnamese, since both looked very much alike. A grizzled Marine settled it for us. He said, "If he is pointing a gun at you, he's VC."

Pure water was a problem, too. We found out how some of the soldiers and Marines solve their problem for a pure drink. The story goes that the general was inspecting an outfit in the boondocks where the water supply was definitely polluted. He asked one of the newer recruits how he treated the water to make it safe. The soldier said. "Well, we get the water out of the river or rice paddy. Then we filter it through a bucket of sand; then boil it; then put in the purification tablets. Then we still don't trust it, so we pour it out and go into town and drink beer."

In Viet Nam I worked in DaNang and was the general practitioner attached to Surgical Team #1. There are always medical problems with surgical cases. For perspective it may interest you to know that the surgical team at DaNang is performing about 1,200 operations per month, of which 450 are major procedures. These operations for the most part are on civilians from an area supporting around a million persons. Most of them are war wounds sustained in crossfire between the Viet Cong, the Army of Viet Nam, and Americans.

While in DaNang we had the dubious pleasure, but certainly the excitement, of being evacuated by Marine rescue helicopter from the rebellious city to the more certain safety of the naval hospital compound. After two days we went back to our posts, though the nurses and other Americans were kept out of the city for a week.

Surgical Team #1 is supervised by Dr. George F. McInnes, a prominent surgeon of Augusta, Georgia, whose father, incidentally, is both a physician and a veterinarian, who at age 85 is still in active practice of both professions in that city.

The weather was hot, as you would expect in the tropics, and we soon came to understand what the natives of India meant when they used to say, "Only mad dogs and Englishmen go out into the noonday sun."

It is my understanding I am to give the KEYNOTE address. I take it that what I say should be the "key" to the remainder of the program, and further, that it should only be a "note." I shall try to make it just that.

I bring you greetings from the American Medical Association, especially from its council on Rural Health, from the new chairman Dr. Ben Saltzman of Mountain Home, Arkansas, and from Dr. Bond Bible, our Executive Secretary in Chicago. I also bring greetings from Dr. Dinh Van Tung, Medicin Chef of the DaNang Civil Hospital in Viet Nam, who personally has attended five cases of human rabies, and from Dr. Anthony G. Brown, an English physician and coordinator of Project Viet Nam who has attended four cases. These men gave me a preview of what the rabies problem is like in Southeast Asia.

It was left to a nurse-technician who has worked in the highlands of Viet Nam near Laos, to state the rabies problem succinctly: "The bats come out of the caves and bite the civet cats and the tigers; the village dogs chase the civet cats and the tigers. If they live, they may get rabies. Then they bite the village cats and the children, and unless these people get the Pasteur treatment they may get rabies . . . ."

There were five human deaths from rabies in South Viet Nam last year that are fully known and documented, perhaps more. By the same population incidence in the United States there would have been 65 cases.

In Viet Nam, by comparison, rabies is no competition for plague, cholera, malaria, typhoid fever, or tuberculosis, but the three Pasteur Institutes at Saigon, Dalat, and Nha Trang gave 12,000 consultations and 7,000 treatments, with the majority of animal cases being found in dogs,

[1]Rural Health Committee, American Medical Association, Boiling Springs, North Carolina.

cats, bats, pigs, and monkeys. There was one case of paralysis, but no deaths from treatments.

One of the reasons I was invited to speak to this meeting is that I am old enough to remember the fear of rabies 50 years ago. I well remember the shrill and awesome cry of "Mad Dog," "Mad Dog" which coursed through the small rural community if a suspected rabid dog was seen. I saw such a dog, and recall it as clearly as if it were yesterday. Only two rows of cotton separated me from him. I remember his wild eyes, slavering jaws, and lurching gate. Foolishly we children tried to throw water on him to see if he really had "hydrophobia." He was found dead nearby the next day.

Then, some physicians treated bites of suspected rabid animals with applications of the "madstone" which was available at Charlotte or Raleigh and could be obtained by sending a telegram. People who could not afford a telegram just boiled their clothes in salt water for about a year. My mother's cousin must have missed a few salt water boilings. He contracted rabies eight months after he was bitten.

The American Medical Association and its Rural Health Council are interested in any-and everything which concerns the health of rural people. One of our objectives for many years has been to work with state and national organizations in specific projects to improve health. We are peculiarly interested in this National Symposium on Rabies because rabies is becoming one of the national health problems coming more sharply into focus each year. Also the sponsoring organizations, the American Veterinary Medical Association and the U.S. Public Health Service, are among our valued advisors. As you know, some of your top men, Dr. James Steele and Dr. Martin Hines and others, have appeared on our national programs, and others have counseled us in many helpful ways. I am grateful your program committee saw fit to invite me to this meeting.

Along with us, you are aware of recent declines in rural populations, the reduction in the number of farm families, and the attendant increase of new forests, new lakes, and wildlife and game refuges. We welcome the provision of more "wide-open spaces" but also know these things bring more animals and with them the potential threat of rabies.

I can assure you we are ready to plan and assist and cooperate and sponsor and give guidance to any of the medical aspects of any program designed to reduce rabies or the threat of it, in animals or man.

It is probably of secondary importance simply to mention incidence. It is interesting, however, that there are approximately 5,000 cases of proved rabies in animals every year, and that these cases are found in badgers, beavers, coyotes, foxes, mice, mink, muskrat, rabbits, raccoons, rats, skunks, squirrels, weasels, wolves, woodchucks, and in all domesticated farm and household animals.

It is important to know that approximately 150 persons have died of rabies in the United States since 1946, the year I began the practice of medicine in Boiling Springs, North Carolina, and that during that year all exposures that brought subsequent deaths were from cats and dogs. But NOW, only 50 percent of the exposures and subsequent deaths are from cats and dogs. The remainder come from bats, foxes, skunks, and other OUTDOOR wildlife animals. In 20 short years the picture has changed from an URBAN to a RURAL RABIES PROBLEM.

As the trend grows, we may even have to change the name of Georgia from the "Peach State" to the "Coon State," because last year out of a total of 123 proved cases of animal rabies in the state 107 were from coons from the Okefenokee swamp. And with a swamp as big as Okefenokee the researchers may have missed a few.

The big swing from domestic to wild animals hinged on the year 1959, and last year all states and territories had wild animal cases except the District of Columbia, Hawaii, Rhode Island, Wyoming, and the Virgin Islands.

You will hear more about it later, but in this overview we must consider rabies as an international problem. It is supranational. A few countries like Australia, Hawaii, and Ireland have never had it. A few others keep it almost totally suppressed, but generally it is prevalent everywhere, from Alaska to Asia, from Lapland to the Argentine. Animal vectors know no national boundaries, and the virus recognizes no national origin.

Having just completed a journey around the earth I can assure you there is much coming and going of men and animals. We have the war, the Peace Corps, exchange students, and tourists, plus all the ramifications of trade and business. Who can say when a boy in Brazil, a man in Mexico, or a girl in Greece may be bitten by an animal and get rabies, and is he or she less important than a similar person in your hometown? This international aspect calls for much study, many records, full cooperation and probably a lot of money.

What shall we do about it? Several things need to be done. May I suggest an immediate goal: GIVE US A BETTER VACCINE. The world waited nearly 60 years for the original Pasteur vaccine to be much improved. We have a better one in the avian vaccines, but you know the complaints. There are too many shots. It hurts too bad. And there are some reactions, still.

We improve our autos and TV sets with new models. It will be completely American to improve the vaccine. Could we set for ourselves this goal: make the vaccine process short, simple, safe, sufficient, and inexpensive?

A second goal: GIVE US A BETTER AND QUICKER DIAGNOSIS. We have advanced from the impoundment of the suspected animal to biological tests, and to finding Negri bodies in the brain, and now to the fluorescent antibody response. Is it unreasonable now to wish for a push-button diagnosis which can be done in the doctor's office or at the local health department, in minutes, so as to relieve the anxiety of some 32,000 persons who take the vaccine each year because they do not now know!

A third thing to do now is to provide, and not only provide but insist upon, pre-exposure treatment of persons in high risk occupations. Make the requirement legal if necessary. For instance, all of YOU. And all other veterinarians, animal and meat men, farmers, hunters, trappers, campers, naturalists, and laboratory and research workers. Also, mail men, electricians, meter readers, spelunkers, lumberjacks, Peace Corps workers, all soldiers and civilians in foreign service, and, to include myself, physicians who make house calls.

Others concerned may or may not be vaccinated, such as physicians, hospital personnel, members of humane societies, conservationists, and key personnel in city, county, state, and federal agencies at all levels. The goal here is for prevention, containment, and complete control.

In this connection we can do a fourth thing. If we immunize enough persons against rabies we can create an adequate source of human anti-rabies hyperimmune serum which is rich in antibodies and is safe. Also, in addition, we might improve the hyperimmune serum we have now from horses. We took the thorns off some rose bushes, and have taken the seed from oranges and melons. If someone will look in the right place he may find a way to take the reactions out of horse serum and leave the antibodies. At this point I would like to compliment the Georgia VMA for its beginnings in producing human hyperimmune serum.

Another thing we can do immediately without waiting for all the answers is to engage in a widespread educational program, translating all the known facts about rabies to the professional people in their language and to the general public in their language. There are at least 100 national organizations which profess to be concerned about the health of rural people. They need the latest information on methods, research, responsibilities, and opportunities for service in this field. This is a "natural" for newspapers, radio, and TV, for women's farm organizations, civic clubs, Boy and Girl Scouts, and hospital staffs. All concerned should be primed for action programs, including more conferences like this at state and local levels.

We have spoken of immediate goals. May I now challenge you to a long range goal: the complete and ultimate elimination of rabies. Impossible, you say? The pages of history are filled with people and nations who did the impossible. The ones who said it was impossible are forgotten.

The answer is not likely to be found in the history of rabies, as interesting and fascinating as those facts may be, nor in our present knowledge, as valuable and helpful as this may be. The riddle will probably be solved along the new frontiers of cellular biology and the biophysics of the cell and its invaders, the viruses. If we spend billions on space, atoms, and electronics in going to the moon, charting a course to Venus, or calculating the energy from quasars, may we not divert a few millions for means and methods to rid this planet of rabies? In fact, some of the new knowledge and techniques gained in these more expensive endeavors may be just what we need. Electron microscopes, computers, and data processing machines and automated laboratories may come up with some astounding answers. The wilderness may become a highway.

Let me challenge you to a program of extended research. Tell us more of the basic nature of viruses, their ecology, habits, likes and dislikes, their molecular structure, and the biological forces which nourish and control them. Know their sizes and shapes and even the nature of their DNA and RNA content. Grow them in or out of animal or man, learn how to manipulate and control them, find out what makes them tick. I know you are doing a great job now, but the world is in a hurry.

Discover for certain all the ways a man or animal can become infected. Master the bat, from the little brown one to the big black vampire.

Tell us how bats can carry and transmit the deadly virus and not themselves be killed by it. Surely this ubiquitous little animal has some secrets we need to know.

Find some way to vaccinate wildlife by introducing vaccine into their food and water (when I was in medical school 25 years ago leading scientists said a vaccine for polio was unlikely and an oral vaccine was impossible). Check on the relationship of Listeria monocytogenes to animals and their viruses, especially in foxes. As one of Dickens' characters said, "something might turn up."

Surely a technology and science which have virtually conquered anthrax, glanders, animal TB, and brucellosis will not stop at rabies. There are nearly 300 other diseases transmitted from animal to man which also cry for control. Surely the same force and will that overcame yellow fever, typhoid fever, diphtheria, and polio will now be brought to bear on this worldwide menace of rabies. Yes, it is RURAL; yes, it is DIFFICULT; yes, it is EXPENSIVE. But if we can eliminate these other diseases; if we can stop the fruit fly, the fire ant, the witchweed, and the corn borer, we can also stop rabies.

We will do it for several reasons. We will do it for medical reasons, because it is humane to prevent what we cannot cure. We will do it for economic reasons, because it costs millions of dollars to lose cattle and to vaccinate animals and people, exposed or not exposed. We will also do it because, like climbing the mountain, "it is there."

We still have the Biblical injunction, in the first chapter of Genesis, to replenish the earth, which, from the reports on the population explossion, we are doing very well. But the same verse goes further. It says "and subdue it. . .and have dominion over every living creature that moves upon the earth . . . ."

I take it this still means the foxes in Virginia and Tennessee, the coons in Georgia, the skunks in Ohio, and the bats which pour out of the millions of hiding places in all the states, bringing the viruses with them. We have quite a lot of subduing and dominating left to do.

For your approval I submit this acrostic:

R esearch, Rural
A nxiety, reduced
B ats, mastered
I mprove vaccines and sera
E liminate rabies all over the world
S ubdue and dominate

I commend you to the task.

RESEARCH

***Robert E. Kissling, D.V.M.*, Chairman**

Kinetics of Rabies Virus Growth in Tissue Culture

Tadeusz J. Wiktor, D.V.M.[1]

I shall concentrate on the work of our group at the Wistar Institute during the past year dealing with various aspects of growth of the rabies virus in tissue culture, its physical characterization, and certain interrelationships with other viruses. Our group, headed by Dr. H. Koprowski, was composed this year of Drs. M. M. Kaplan, R. Maes, and myself.

Many tissue culture systems of cells from different organs and different animal species were investigated, and practically all of them were susceptible to rabies virus infection to a lesser or greater degree. However, we have concentrated mostly on two systems of contrasting degrees of susceptibility, the rather resistant human diploid cell strains (HDCS) (1) and the very susceptible baby hamster kidney cells (BHK) (2). Another reason for studying the comportment of rabies virus in HDCS is the possible use of this cell strain for human vaccine production.

First, just a few words on general and well-known features characterizing infected rabies tissue culture. One of the most important, and also most frustrating, characteristics is the replication of the virus without cytopathic effect (CPE). This can be demonstrated with great ease by maintaining rabies infected tissue cultures for many generations by culture splitting and cell transfer, after dispersion with trypsin. The presence of the virus can be demonstrated by infectiousness in animals, the presence of fluorescing antigen (FA) and specific rabies inclusions.

Depending on cell systems and strains of rabies virus, different types of chronic infections can be established. A true carrier system can be obtained, for example, in HDCS infected with Pasteur strain of rabies virus in which a low level of infection with 2 to 10 percent FA cells will persist for as many as 30 generations during an entire life span of HDCS culture.

The same HDCS cells, infected for instance with PM strain of rabies, will show a 100 percent infection after 10 to 15 passages, and eventually will lyse. In order to maintain this system, new noninfected cells must be added at each passage level (3).

A different type of culture can be obtained with RE (rabbit endothelium) cells infected with CVS virus (4). All cells will show the presence of FA after a few passages, and the culture can be maintained without adding any new cells for as many as 200 passages during a period of over 2 years. After about 100 passages, however, infectious virus for animals and other tissue culture systems could not be demonstrated any longer.

With all our present knowledge and experience with rabies infected tissue culture, we still cannot present a true growth curve of rabies virus in the sense of a single step growth curve as demonstrated for many other viruses because of the difficulty of achieving 100 percent synchronous cell infection.

Let us now look at some aspects of the kinetics of rabies infections. Adsorption and penetration of rabies virus is extremely rapid. After a second of contact, virus cannot be removed from cells even by repeated washing; and after a minute of contact, some virus particles will have already penetrated the cells beyond the reach of neutralization by antirabies serum (5).

The percentage of infected cells is generally low for HDCS cells and greater for BHK cells, but never reaching a 100 percent FA in a period of 24 hours, despite the fact that input multiplicity used was at least five mouse infected units per cell. Evidently some factor must be interfering with adsorption and penetration.

Working on this basis, we tried to improve the efficiency of attachment and penetration of the virus. It had been demonstrated that treatment of cells with polycations can improve efficiency of polio RNA infection (6). We therefore tried various polyions. As represented in Table 1, treatment of cells with four different substances can modify efficiency of rabies infection in HDCS.

It seems that action of the polymer is related to the ionic charge. DEAE and protamine sulfate, which possess a positive charge, increase the percentage of infected cells, whereas dextran sulfate and heparin, with negative charges, will decrease the efficiency of rabies virus infection.

We then concentrated mostly on DEAE and studied different methods of application. Table 2

[1]The Wistar Institute, Philadelphia, Pennsylvania.

shows that there was no difference between pretreating cells and adding DEAE to the virus inoculum before infection of cells. The treatment of cells with DEAE after virus adsorption was without effect.

Table 1.–*Action of polyions on penetration of rabies virus in HDCS*

Polyion	Ionic charge	Concentration γ/ml	Rabies FA percent 72 hours postinfection
DEAE Dextran[1]......	Positive	100	37
Protamine sulfate....	Positive	1000	24
Dextran sulfate......	Negative	100	3
Heparin............	Negative	500	1
Control............	....	...	6

[1]Cells treated for 1 hour before infection with virus.

Table 2.–*Time factor in DEAE-d action on rabies virus penetration in HDCS*

Treatment with DEAE-d 100 γ/ml	FA
Before virus adsorption...........................	[1]12
During virus adsorption...........................	13
Immediately after one hour adsorption	2
Four hours after virus adsorption.................	3
Control no DEAE-d treatment.......................	3

[1]Percent fluorescing cells 72 hours after infection.

If the system is used in BHK cells, which as I told you before are much more susceptible to rabies infection, the following results are obtained (Table 3): Addition of 200 or 50 gamma of DEAE to the virus inoculum achieved for the first time 100 percent cell infection in 24 hours. The difference in percentage of FA was also demonstrable in infectivity for mice. Non-treated cells showing 20 percent of FA gave us $10^{3.6}$ LD_{50} in contrast to $10^{4.6}$ in DEAE treated cells.

Table 3.–*Enhancing action of DEAE-d on penetration of rabies virus in BHK-21 cells*

DEAE-d γ/ml	Rabies FA[1]	Mice LD_{50}[2]
200	100	4.4
50	100	4.6
....	20	3.6

[1]Percent fluorescing cells 24 hours after infection.
[2]Tissue culture medium 24 hours after infection.

Of particular interest from the standpoint of kinetics of rabies virus infection was the fact that, with synchronous infection established with DEAE, FA antigen was first observed 8 to 9 hours after infection of the cells, and by 12 hours all cells showed FA, indicating that all cells had been infected with rabies at the same time. This does not mean, of course, that mature infective virus was produced by this time. In fact, mouse infectivity tests could not distinguish any increase in infective virus particles before 15 hours after infection.

Evidently this can be criticized by saying that the mouse inoculation of tissue culture tests are not sensitive enough to demonstrate small variations in amounts of infective virus, but in the absence of other tests we must accept provisionally the interpretation I have given.

Some limited studies on anti-metabolites were made in order to determine various characteristics of the replication of rabies virus (Table 4). Of the DNA inhibitors shown here, only 5-fluorourocil (FU) and cytosine arabinoside (CA) had an inhibitory effect. The mechanism of action of CA is not yet well understood, and studies are being continued. BUDR results shown in this table are mainly a confirmation of Kissling's (7) and Hamparian's work (8). This shows clearly that rabies virus should be included in the group of RNA viruses.

Table 4.–*Effect of various anti-metabolites and analogues on rabies virus replication in BHK-21 cells*

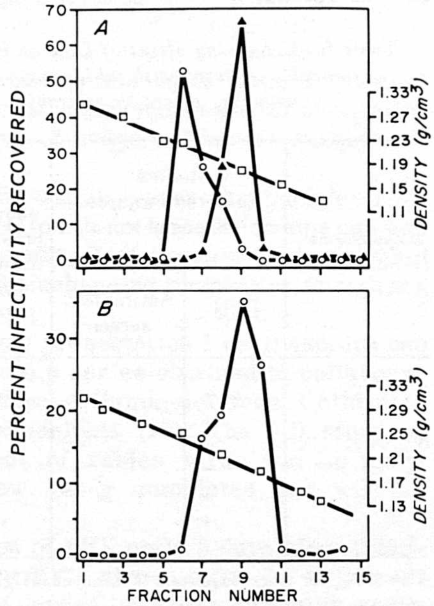
Substance	FA inhibition
DNA Inhibitors:	
Actinomycin D...........................	–
Mitomycin C	–
BUDR (5-bromo-deoxyuridine)...........	–
FU (5-fluoro-uracil) secondary effect	+
Cytosine arabinoside	+
RNA Inhibitors:	
HBB (2-a-hydroxybenzyl-benzimidazole)...	–
Guanidine HCl..........................	–
FU (5-fluoro-uracil) primary effect..	+
Amino Acid Analogues:	
Fluorophenylalanine	+

Some substances known to inhibit some RNA viruses were without effect on rabies virus replication.

The amino acid analogue fluorophenylalanine inhibited rabies virus replication, and this action could be reversed by addition of phenylaline.

With the collaboration of Mr. R. Neurath, the density of rabies virus was determined by cesium chloride density gradient centrifugation (Fig. 1)(9). This revealed a heterogeneous population of virus particles, the majority showing the density of 1.20 g/ml. Fraction 7 and 10 were centrifuged separately in cesium chloride, under the same conditions as was original material, to exclude the possibility that the broad peak of infectivity could have been an artifact due to experimental conditions. Results shown in this top curve suggest that heterogeneity seems to be an intrinsic property of the virus population.

Figure 1.–*CsCl equilibrium density gradient centrifugation of rabies virus.*



Fraction 1=bottom; fraction 15=top. Part A: Recentrifugation of fractions No. 7 (o) and 10 (▲) from Part B (centrifugation of infectious tissue culture fluid).

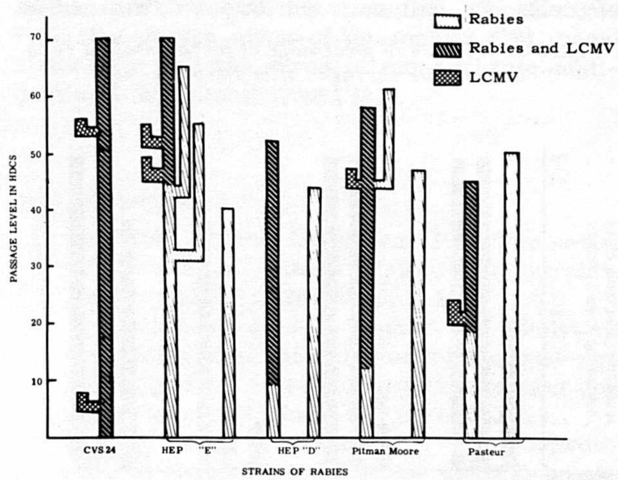
□ *Density* ○▲ *Infectivity*

The sedimentation coefficient of 600 S was calculated for rabies virus from results obtained by rate zonal centrifugation in preformed sucrose gradients. In addition, sedimentation coefficients of about 23 S and 10 S were calculated for two soluble rabies antigens present in infected tissue culture fluids, and they showed a density of 1.26 g/ml in cesium chloride solutions.

You are certainly familiar with the question of contamination of some of our tissue cultures with the virus of LCM (10). This question has a very important practical aspect in connection with preparations of antirabies vaccines. We cannot even claim priority for observing this misfortune, since Casals and Webster made similar observations 26 years ago (11). The presence of LCM was also detected in some of the purified rabies preparations obtained by Sikes (12).

The virus of lymphocytic choriomeningitis was isolated on six occasions from human diploid cell strains infected with different strains of rabies virus (13). As it appears from Figure 2, the contamination with LCM occurred very early and probably at the first passage level in cultures infected with CVS virus, and this partnership of

Figure 2.–*Presence of LCMV in rabies infected tissue cultures.*



two viruses could be maintained in the same cultures for as many as 70 serial cell transfers, during a period of more than a year.

In other cultures the presence of LCM could be detected at different passage levels, and symbiosis of two viruses could be maintained for many generations.

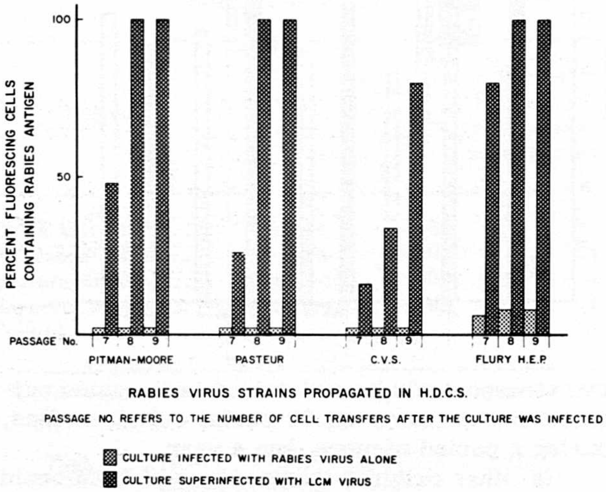
Since the presence of LCM in mouse breeding colonies is not uncommon, it seems likely that the LCM virus entered the CVS stock from the mice in which this strain of virus was propagated for many passages, and, after infecting the cell culture of CVS series, LCM was transmitted to other cultures by aerosols during manipulations.

As demonstrated also in this figure it was possible to obtain LCM-free rabies cultures when new passage series were started from material below the level where the LCM virus was first detected. With other strains, culture series were started again from original virus pools and were propagated for 40 to 50 cell transfers without appearance of LCM antigen.

These results indicate that LCM virus was a constant partner of rabies in many tissue cultures studied in our laboratory. The nature of this association has been further investigated (14). Cultures of human diploid cell strains were infected with four strains of rabies and maintained by cell transfers every 3 to 4 days. No CPE was observed, and the proportion of cells showing the presence of rabies FA antigen varied from 2 to 8 percent at each transfer.

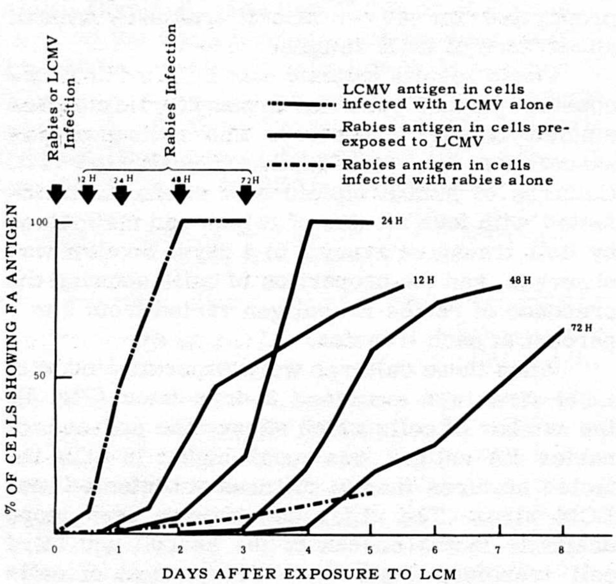
When those cultures were superinfected with LCM virus and examined 3 days later (Fig. 3), the number of cells which showed the presence of rabies FA antigen was much higher in LCM infected cultures than in cultures not infected with LCM virus. The difference became even more dramatic in the course of the second and third cell transfers when 80 to 100 percent of cells in LCM infected cultures showed the presence of rabies FA-antigen, in contrast to 2 to 8 percent of cells in cultures not infected with LCM.

Figure 3.—*Increase in percentage of rabies infected cells one or more passages after superinfection with LCM virus*



Studies were then made to determine the optimal conditions for this LCM enhancing action on the rabies virus. Figure 4 shows the results of pre-infection of cultures with LCM 12, 24, 48, and 72 hours before infection with rabies virus. After we had first determined that the best enhancing effect was observed by LCM infection preceding rather than simultaneous with, or subsequent to, an infection with rabies virus, we found that the maximum response was obtained when LCM was used 24 hours before rabies at a time when 20 to 30 percent of cells showed LCM FA-antigen.

Figure 4.—*Enhancing effect of LCM on rabies multiplication*



Two experiments are represented in Table 5. First, we determined that the increased proportion of cells showing rabies antigen was actually accompanied by a greater yield of infective rabies virus. In the second series of experiments, HDCS cultures chronically infected with rabies virus were exposed to LCM in the presence of antirabies serum free from LCM antibodies. The cells were transferred 3 days later. For control purposes, cells were also transferred from cultures treated with antirabies serum in the absence of LCM virus, and from cultures exposed to LCM but not treated with antirabies serum.

Table 5.—*Enhancing effect of LCM on HDCS cultures chronically infected with rabies; prevention of the enhancing effect by antirabies serum*

Experiment Number	Rabies infected cultures exposed to: LCM	Antirabies serum	Cells showing presence of rabies antigen *percent*	Yield of infectious virus[1]
A	–	–	3	$10^{-1.7}$
	+	–	[2]100	$10^{-4.0}$
B	–	–	18	Not tested
	–	+	10	Not tested
	+	–	[2]100	Not tested
	+	+	[2]10	Not tested

[1]In LD_{50} for mice injected intracerebrally.
[2]At the first cell transfer after exposure to LCM.

The results indicated that when superinfection with LCM increased the number of cells showing the presence of FA rabies antigen from 18 to 100 percent, the presence of antirabies serum virtually abolished the enhancing effect of LCM virus. This indicated that the enhancement effect was brought about by infection of new cells with rabies virus, and not by completion of growth cycles in already injected cells.

Finally, it was important to determine whether living LCM virus was required to exert the enhancing effect. Table 6 shows that UV inactivated LCM was also effective in provoking the enhancing effect although to a lesser degree than was the live LCM virus. The exposure time to UV was 60 to 180 seconds, and this dose was sufficient to inactivate the LCM virus completely. The enhancing effect could be reproduced in RE, RK13, mouse tumor cells TCBS, Nil 2 cell line of hamster embryo, but not in BHK cells. Incidentally, we were unable to show an enhancement effect of LCM on rabies virus in vivo in mice.

One possible explanation which we favor at the moment is that the enhancing effect is exerted by

Table 6.–*Enhancing effect of UV inactivated LCM virus preparations on rabies virus*

Pre-exposure of cultures infected with rabies virus	Cells showing presence of FA rabies antigen[1] *percent*
LCM	100
LCM-UV Inactivated	22-36
Control	8

[1]72 hours after rabies infection.

a factor produced by the LCM virus or present on its protein coat, which increases the absorption and penetration of rabies virus on susceptible cells.

It seems certain, however, that the infectivity of LCM preparation is not a condition sine qua non for the enhancement effect, because UV inactivated virus retains the enhancing properties though at a reduced level.

To finish my presentation I shall mention two photographs from a series obtained in collaboration with Dr. Klause Hummeler from Children's Hospital of Philadelphia (15). The full story on the development of rabies virus and its morphology is now being completed and will be published soon.

In a section of BHK cells 5 days after infection with Flury HEP virus, there is an almost crystalline-like array of virus particles and a very large number of particles observed throughout the cytoplasm of the cell. It must be remembered that in the presence of such infection, the infective titer in mice and tissue culture remained still on the low level, not exceeding 1 to 5 mouse infective doses per cell. There are two possibilities to explain this fact. First, the virus particles represent either noninfective incomplete or inactivated virions, and some as yet unidentified factor is interfering with the efficiency of virus maturation. Secondly, a mouse infective dose could represent a tremendous number of virus particles; this is not at all unlikely. For example, we have roughly calculated that with DEAE, one mouse infective unit is sufficient to infect 70 tissue culture cells, and we have no idea how many virions are necessary to infect one tissue culture cell.

A second picture obtained after negative staining with PTA revealed an unsuspected architecture of rabies virus particles, which will oblige us probably to declassify rabies virus from the myxovirus genus where it was formerly grouped with influenza, parainfluenza, NDV, and other viruses. It is now clear that rabies virus falls morphologically at least in a group comprising the virus of vesicular stomatitis (16), lettuce necrotic yellows virus (17), plantin virus (18), the sigma virus of drosophila (19), cocal virus (20), and the virus of hemorrhagic septicemia of the rainbow trout (21).

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Purified Rabies Vaccine of Mouse Brain Origin

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A purified rabies vaccine was prepared from infected suckling mouse brains using ECTEOLA cellulose chromatographic procedures. The virus was inactivated with beta propiolactone (1:10,000) at 4°C for 48 hours and dialyzed overnight in 0.01M sodium phosphate buffered water, pH7.2. The 100 ml (1:25 dilution) of purified virus was concentrated to 10 ml using Carbowax. Five percent sucrose and .0075 percent glycine were added as stabilizers, and 1000 units of penicillin and 2.0 mgm of streptomycin per ml as well as a 1:10,000 concentration of merthiolate were added as preservatives. Half of the resulting vaccine was lyophilized in 1.0 ml quantities and maintained at 4°C. The other half was kept in suspension at -20°C until tested.

This purified vaccine contained 62 times less phospholipid than the duck embryo vaccine and 383 times less than the currently used Semple vaccine. It contained 36 times less nitrogen than the DEV and 40 times less than the Semple vaccine. No cholesterol, mono or triglycerides, nor any free fatty acids were detected in the PRV, but each of these was present in the other vaccines. A trace of diglycerides was present in all three vaccines.

The PRV passed the Habel and NIH potency tests; the other vaccines were less potent than the PRV in both tests. The PRV protected guinea pigs better than the other two vaccines following 14 daily doses of vaccine. The SN antibody titer of guinea pigs vaccinated with 5 to 14 daily doses of PRV was consistently higher than that detected in guinea pigs vaccinated with either the DE or Semple vaccines. No encephalitogenic factor was detected in guinea pigs inoculated with the DEV or PRV.

Four professional members of the Rabies Control Unit have received injections with this new PRV vaccine. No pain on injection or reaction was noted. One person who had received other types of vaccine and never developed detectable rabies antibody responded with a titer within one week after receiving the PRV.

The complete paper on the development and testing of this purified rabies vaccine has been prepared for publication in a scientific journal.

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Pathogenesis of Rabies in Rats

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The pathogenesis of "street" rabies virus was investigated in rats. Previously reported work with fixed virus (Bull. WHO 33:783-794, 1965) had demonstrated that virus passes through either the Schwann cells endoneurium or associated tissue spaces of the sciatic nerve after inoculation into the footpad. Virus was first noticed in the lumbar segment of the spinal cord.

Experiments with "street" virus support the earlier results with the fixed strain. Virus is found only in the inoculated foot of rats killed immediately after inoculation. No virus could be demonstrated in rats killed 1 or 3 days after inoculation, but one of four rats killed 6 days after inoculation had virus in the lumbar and thoracic segments of the spinal cord, as shown by mouse inoculation and the fluorescent antibody technique. No virus was seen in peripheral nerves during these periods. After 9 days, many more rats showed presence of virus in numerous neural structures and organs. The spread of virus from the central nervous system to the salivary glands, brown fat, and lungs appeared to be centrifugal. Incubation periods in a control group of rats were 12, 19, 21, 32, and 35 days.

Sciatic and saphenous neurectomy before inoculation proved to be a saving procedure in all rats so operated, as shown previously with fixed virus. Neither the removal of the perineural structures (epineurium, perineurium, or perineural epithelium) nor demyelination (proven histologically by absence of axons and myelin) was effective in significantly reducing mortality after challenge, thus again incriminating the nerve fasciculus as the route of ascent of rabies virus.

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Chronic Rabies Infection

J. Frederick Bell, M.D.[1]

Because of time limitations, this review of chronic rabies must be selective rather than comprehensive. Anyone particularly interested in certain aspects of the subject will find them more extensively treated in some of the bibliographic references. I have deleted discussion of rabies in animals such as opossums and chickens that are naturally rather refractory.

My use of the terms "chronic" and "infection" are liberal, but the usage is not completely arbitrary; infection has previously been defined as mere presence of virus. (26).

Dogs. Rabies in dogs is one of the few diseases with duration of clinical signs defined by statute. When a suspect dog inflicts a bite, it is ordinarily taken into custody and held for 10 to 14 days on the assumption that survival after the saliva becomes infectious cannot exceed that period.

Three syndromes are distinguishable in naturally infected dogs. In one form, death occurs suddenly without characteristic or premonitory signs, or death may occur suddenly during an initial convulsive seizure. In the more characteristic furious syndrome, duration of illness is known to be as long as 2 or 3 weeks (20) but, in the typical case, death occurs well within the usual 10-day period of observation. The third form of infection, dumb rabies, which occurs in dogs and also commonly in other species, such as cattle, is characterized by rather rapid progression of paralysis: characteristically, death occurs within 3 days.

In spite of legal limitation of the survival period, the idea that rabies may occur as a nonfatal infection in dogs is not a new one. Competent early observers, including Pasteur (22), made no claims of inevitability of death of dogs with the disease and actually reported the opposite. Just how the common belief in inexorable lethality became so well established is uncertain. Recent studies by Andral and Serie (1) in Ethiopia have convinced them that chronic rabies and recovery from rabies are not only possible, but may be the common forms of disease in dogs. Others—see discussions in Bell (6) and Martin (25) —have made observations that they interpret as nonfatal carrier rabies infections in dogs.

There seems to be little expressed doubt among experienced investigators of dog rabies that survival or protracted infection may occur at times. Nevertheless, its occurrence is generally considered rare in this country and, therefore, noteworthy (35). The fact that investigators have failed to record the common occurrence of chronic rabies in dogs in this country in the past is insufficient evidence that it does not exist—medical history is redolent with failure to note the obvious. There is also a possibility, if not a likelihood, that evolutionary change has occurred, either in the virus—as has been so well exemplified recently by the myxoma virus in Australia (24)—or in the canine population as in Africa during a long history of experience with the uncontrolled disease.

Several forms of "chronic" rabies have been reported:

(1) Delayed onset: Various sources give different figures for minimum, average, and maximum incubation periods; all of them cannot be given here. The committee on animal health of the National Research Council (12) states that rabies in dogs may occur 10 days after exposure, but that 21 to 60 days is the usual range. Some of the committee's most reliable data on deferred onset were obtained on animals in quarantine. Of 16 dogs that developed rabies in quarantine, 4 became ill between 4 and 6 months after entry and one developed rabies at 6 months and 24 days. These were minimum times, of course, because the dates of exposure were not known. Use of the term "incubation period" is probably misleading here, as it is in so much of the literature on rabies, because of the implication that there is a steady, slow, but silent proliferation of virus from the time of exposure to the time of clinical onset. However, evidence that rabies virus can behave as a "slow virus" is inadequate, and it would seem rather that much of the silent period in cases of deferred onset is imputable to an inert

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state of the virus. When this unmodified neurotropic virus is transferred in more than minimal quantity directly from diverse natural sources to the susceptible CNS tissues of susceptible animals, a rather uniform "basic" incubation period usually occurs.

(2) Clinical disease followed by clinical recovery: Van Rooyen and Rhodes (39) cite several reports of recovery of dogs from rabies. A recent occurrence of this kind has been reported by Starr et al. (35). However, in the absence of definitive studies on isolation of virus from saliva during illness, there is room for doubt in the interpretation of signs of illness as we have noted in our studies on cats (unpublished). In the case reported by Starr, rabies virus was isolated from the brain after apparent recovery. Failure to isolate virus from the brain after apparent recovery would not be a refutation of diagnosis, inasmuch as "autosterilization" (23) of brain is a common occurrence after several days of illness (19). This development could justify a question as to whether the virus itself or reaction to it is responsible for death. Inquiry into this question would be of at least academic interest. Andral and Serie (2) believe that recovery from rabies is the most logical explanation of the refractory state of challenged dogs in Ethiopia.

(3) Clinical disease of long duration: There are reports in the foreign literature of a protracted infected state in dogs. Broz and Phan Trinh (10) record the transmission of rabies to 2 of 10 persons bitten by a dog over a period of 26 days. The dog was killed by the owner, because of its predilection for biting, 22 days after the first and 19 days after the second fatal bites.

(4) The healthy carrier state: Thiery (37) has reported recurrent rabies and healthy carriers, and Yurkovsky (42) observed 21 fatal cases of human rabies from bites of 21 dogs, all of which appeared healthy. Svet-Moldavskaya (36) referred to earlier observations of similar occurrences.

Vaccination of dogs is prohibited in Germany because of purported development of chronic rabies in such animals when exposed, but the WHO Expert Committee (15) found no evidence of the existence of a street virus carrier state in dogs immunized with rabies vaccine. Nor is there any reason to believe that live attenuated virus vaccine constitutes a danger for man or animals through transmission from saliva of the vaccinated dog.

There appears to be little doubt that rabies-infected dogs may survive the disease, but the incidence, and variations in incidence, are not known. If chronic or carrier rabies is a common occurrence, it is undoubtedly important in the epizootiology and epidemiology of the disease and a factor to be reckoned with in prophylaxis and control. In view of strong suggestions but present uncertainty of high incidence, establishment of infrequent occurrence would also be desirable.

Bats. Rabies infection as a chronic disease of tropical bats (30) is so well known that there does not seem to be much point in extended discussion here. In spite of its being well documented, basis for this peculiar parasite-host relationship has not been completely elucidated, although Johnson (18) has produced asymptomatic infection in dogs by inoculation of virus derived from vampires. There remains an inference that some peculiarity of the host or of the method of its infection is responsible for the relationship. This persistent infection in a transmissible state is chronic infection in the generally accepted sense; i.e., an apparent continuous propagation or persistence of viable virus within the host.

The chronicity of rabies in tropical bats is a major factor in their great importance as vectors to man and especially to cattle.

We (7) have studied rabies in Montana and Idaho and have found 36 naturally infected bats since 1954. Our assumption has been that chronic carrier rabies occurs in northern insectivorous species as well as in fruit-eating and vampire bats. However, in spite of our efforts to show long survival with continuous infection, we have been unable to do so. In fact, we have not even been able to prove survival after natural or experimental infection. These limited data do not prove that chronic infection does not or cannot occur in bats in the northern United States. At the Southwest Rabies Investigations Station, of the Communicable Disease Center (University Park, N.M.), apparently normal insectivorous bats have been found with virus in the saliva but not in the brain (38). Stamm et al. (34) found Negri bodies in the brain of a bat that did not succumb to experimental rabies infection.

In the case of the vampire, of course, increase in ferocity or stimulation to bite as the result of infection is not necessary for passage of the virus, because the vampire bites to feed. Some other species are normally carnivorous, and pernicious quarrelsomeness is observable in colonies of normal insectivorous bats. These activities could also lead to transmission without specific incitement. The general applicability of the observations of transmission without contact, as has been demonstrated in the laboratory (3) and in certain caves (12), is not yet established.

Other Wild Animals. In the United States, rabies is now recognized more frequently in wild animals than in dogs or cats. Foxes and skunks are particularly well known vectors in North America, and wolves, foxes, jackals, mongooses, and meerkats are recognized as important vector-reservoirs in other countries.

There is some evidence that rabies may occur in some of these species as a nonfatal infection. Martin (25) reviewed that evidence, and other data have been obtained more recently. We may categorize the data as follows:

1. Isolation of virus from animals that appear normal.
2. Detection of Negri bodies in killed animals from whose tissues virus could not be isolated.
3. Presence of neutralizing antibodies in the serum of animals that appear normal.
4. Presence of specific neutralizing capacity of brain tissue.
5. Individual animals (of susceptible species) that are refractory to intracerebral challenge.

Data of this kind are often strongly suggestive of recovery, but interpretation has been cautious because of the fact that both virus and serum antibodies may be found in animals just prior to onset of illness. We had assumed in the past that cerebro-neutralization was simply a reflection of the serum neutralizing capacity (16, 27), but recent studies on rabies-infected mice have revealed that in that species, at least, the phenomena are unrelated (8). Thus, a high cerebro-neutralization titer occurs only after infection, not after vaccination, and it does not develop in appreciable degree until late in infection (which may be subclinical). Cerebro-neutralization appears to correlate well with the refractory state demonstrated by intracerebral challenge (6). It would seem, therefore, that demonstrations of either the refractory state or of high cerebro-neutralization titer (11) in normal-appearing animals may be interpreted as evidence of survival.

I believe there has not yet been a demonstration of infectious saliva in naturally infected wild animals prior to or during the occurrence of the resistant state, but experimental infection of skunks and foxes has demonstrated that all phases of the infection may be prolonged (29). Two skunks died 137 and 177 days after inoculation. One skunk shed large amounts of virus in its saliva 18 days before death, and one fox was clinically rabid for 17 days.

Experimental Animals. Chronic rabies in animals infected experimentally has been noted repeatedly. Long incubation periods are well known when unmodified street virus in very low titer is inoculated intracerebrally, and wide variations in incubation period are common when virus is inoculated peripherally. Soave and associates (32, 33) have demonstrated that cortisone or stress may activate the infection in cavies. Long duration of illness after onset is also well known but, again, criteria of illness are moot.

Vaccination is thought to prolong the incubation period (14), and survival of vaccinated animals after definite onset of illness is seen frequently by those who test the potency of vaccines. Barme (5) has noted that crude antiserum also prolongs the incubation period.

We also see very frequent survival of mice that receive intraperitoneal injections of low-passage virus from diverse sources (6). Ordinarily half or more of the animals that develop typical signs of rabies after the injection will not succumb but survive with permanent, more or less severe sequelae. In the early stages of the manifest disease, virus can be obtained from the brain, but at about the seventh day of illness, incidence of demonstrable infection in brains of such mice starts to decline. Mortality also declines at about that time, and subsequent deaths are more logically ascribed to the permanent sequelae rather than to the infection itself. Nevertheless, we have occasionally isolated virus some weeks after onset, and Webster (40) and Gorshunova (17) have found virus in brains of mice and of rats, respectively, months after injection. These occurrences suggest the possibility of tolerance, as in LCM virus infection, or latency, as in herpes infection (28), but there is no convincing proof of the occurrence of those phenomena in rabies.

Rats (17), cavies (2), and rabbits (39) infected experimentally have yielded evidence of protracted survival. In the rabbit, a wasting form of illness may ocur, or death may occur quite suddenly after a long period of freedom from signs of illness. Wasting of muscle tissue has also been seen (20) in mice inoculated with virus isolated from the salivary glands of a spotted skunk and propagated in tissue culture.

Man. Although man is undoubtedly the most carefully observed of all victims of rabies, less is known about chronic rabies or recovery from the disease in this species than in any of the domestic or experimental animals. One reason for this deficiency is the relative infrequency of rabies in man in areas with modern facilities for thorough study. Other reasons include the traditional belief in certain death from rabies and the difficult differential diagnosis of postvaccinal encephalomyelitis (19). Survival after onset of rabies is likely to be noted and reported only by someone who believes that it is possible. Documentation will have to be exceptionally convincing to overrule established belief.

Extreme variations in one phase of the infectious process, the incubation period, are well recognized and are in part dependent on the site of entrance of the virus. Selimov (31) has recently reported two instances of rabies with apparent incubation periods of over 2 years.

Isolation in Russia of rabies virus from patients suffering from multiple sclerosis has been rumored for at least 10 years. Evidence that this relationship may not have been coincidental was obtained by a committee that visited Russia recently (9). Nevertheless, it seems hardly credible that rabies virus is the specific etiologic agent of multiple sclerosis, or even a common agent, if there are several.

Chronic (Carrier) Infection of Tissue Cultures. Rabies virus could qualify as the type virus for indolent, harmless infection of tissue culture. We have one bottle of infected hamster kidney cells that has produced virus continuously for 23 months; the unstained cells are indistinguishable from those in an uninfected control culture of the same age.

Rabies virus has been grown in tissue culture for 30 years (21, 41), and a recent spate of activity in this field has succeeded in adapting the virus to various cells to an extent that permits proliferation in sufficient quantity for use as vaccine. Manipulation has also resulted in the development of systems that regularly display cytopathogenic effects.

In spite of apparent absence of CPE in some systems, demonstration of inclusion bodies by staining of infected cells testifies to an apparent nonvital alteration of cellular activities (4). Pertinence of these observations of infection in vitro to the silent presence of virus in long incubation periods has not been shown.

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EPIDEMIOLOGY

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Sporadic Cases of Rabies in Wildlife: Relation to Rabies in Domestic Animals and Character of Virus

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The urban or epidemic type of rabies as it occurs in dogs overshadows the sporadic cases of rabies in wildlife which are so important to our understanding of the source of rabies virus in nature. In a region where cases of rabies are observed in wildlife at intervals of a few years and there is no other evidence of the presence of the disease, one can assume that a resident species of wildlife is able to perpetuate the virus as an asymptomatic infection.

The occurrence of sporadic cases of rabies in man in the Southwestern United States from the bite of the spotted skunk, Spilogale putorius, is perhaps the most spectacular illustration of rabies derived from wildlife. A woman died of rabies in California in 1954 after she had been bitten by a spotted skunk when on a hunting trip with her husband (1). There had been no known cases of rabies in dogs or wildlife in this region for many years. The virus obtained from the spotted skunk, and the human case infected by it, was unusual in that the disease produced by it in mice was characterized by a long incubation period, and the cytoplasmic inclusion bodies found in the brains of the experimentally infected mice were different from the Negri bodies found in mice infected with the virus obtained from dogs. Subsequently, an effort has been made to isolate rabies virus from spotted skunks and to look for variants of rabies virus in wildlife which show a relatively low pathogenicity for mice. Although more than 1,500 skunks have been diagnosed as rabid by laboratory examination in California during the period 1935-1965, less than 10 of these were known to be spotted skunks. The rest were striped skunks, Mephitis mephitis. The population of spotted skunks in the endemic foci of rabies in California is as high as or higher than that of striped skunks, but the spotted skunk is not involved in the epidemic cycle of the disease. Only two strains of rabies virus have been obtained from spotted skunks since 1954. One of these was M400, which was killed in Glenn County on October 14, 1957, when it attacked a dog in daytime. The other was M1953, which was killed in Tehama County on January 15, 1960, when it attacked a dog in daytime. In both instances the submaxillary salivary glands had a titer of $10^{-7}/0.015$ ml when tested in infant mice.

There are isolated cases of rabies in striped skunks, but in addition there have been many regional epidemics of rabies in these animals. During such epidemics skunks are found wandering about aimlessly in daytime and otherwise acting abnormally, and carcasses of skunks are found on the roads and in the fields. As soon as a few cases of rabies have been identified by laboratory examination, further testing is limited to instances where a specific diagnosis is needed because of suspected human exposure to rabies. About 40 percent of the cases of rabies in striped skunks were missed by the Negri body test as shown by virus isolation studies in adult mice. We know now that some strains of rabies virus found in skunks would have been missed by both the Negri body examination and the test for virus in adult mice. The fluorescent rabies antibody (FRA) test and the use of the infant mouse as the test animal for isolation of rabies virus have made it possible to recognize natural strains of low virulence, and it is such strains that one would expect to find in the longterm reservoir host of the virus.

The statistics on rabies by counties offers one method of illustrating the ecology of rabies in wildlife. Table 1 gives the statistics on rabies for Napa County, California, for the period 1931-1965. This is a good example of sporadic cases of rabies in skunks, foxes, bobcats, bats, and domestic animals. During 1955 - 1956 and again from 1962 to 1965 the disease occurred in epidemic proportions in striped skunks. It is evident that dogs and foxes were not responsible for maintaining the virus in Napa County. Table 2 gives the statistics on rabies for Sonoma County, California, for the period 1940-1965. Napa County

[1]Arthropod-borne Virus Studies, California State Department of Public Health, Berkeley, California.

Table 1.—*Animal rabies in Napa County, California, 1931-1965*[1]

Year	Total	Domestic			Wildlife		
		Dog	Bo-vine	Other	Skunk	Fox	Other
1931	1	...	...	......	1	...	....
1932	1	1	...	......	.....	...	....
1933	2	1	...	......	1	...	....
1934	.....	...	...	......	.....	...	....
1935	.....	...	...	......	.....	...	....
1936	.....	...	...	......	.....	...	....
1937	.....	...	...	......	.....	...	....
1938	.....	...	...	......	.....	...	....
1939	.....	...	...	......	.....	...	....
1940	.....	...	...	......	.....	...	....
1941	1	1	...	......	.....	...	....
1942	1	...	...	......	1	...	....
1943	1	...	...	......	.....	...	1 squirrel
1944	1	1	...	......	.....	...	....
1945	.....	...	...	......	.....	...	....
1946	.....	...	...	......	.....	...	....
1947	3	1	2	......	.....	...	....
1948	3	...	1	......	.....	2	....
1949	2	...	...	1 cat..	.....	1	....
1950	2	1	...	......	1	...	....
1951	.....	...	...	......	.....	...	....
1952	5	2	...	1 cat..	2	...	....
1953	2	...	...	......	1	1	....
1954	8	2	...	......	2	3	1 bobcat.
1955	26	1	2	......	19	4	....
1956	19	1	1	......	17	...	....
1957	7	...	...	......	5	2	....
1958	10	...	1	1 cat..	5	2	1 bobcat.
1959	5	...	1	......	2	...	2 bats...
1960	3	...	...	......	3	...	....
1961	3	...	...	......	3	...	....
1962	19	...	...	......	18	1	....
1963	42	1	1	1 horse	39	...	....
1964	25	...	3	1 cat..	19	...	1 bobcat, 1 bat ..
1965	24	1	5	......	16	...	2 bats...

[1]Source: Rabies, California Statistical Report Tables 1922-1965

has relatively few dairies, while Sonoma County has a large dairy industry. This explains the higher incidence of cattle rabies in Sonoma County. There were sporadic cases of rabies in skunks, foxes, bobcats, raccoons, bats, and domestic animals. During some years the only cases of rabies recognized were those in cattle. There was a small epidemic of rabies in skunks and foxes in 1950, and from 1960-1965 there was a migrating epidemic of rabies in skunks.

The biome is similar in Napa and Sonoma counties. There are coastal mountain ridges interspersed with valleys containing rivers and creeks, and there is a large population of both striped and spotted skunks in these counties. In some cases it was known that skunks had been

Table 2.—*Animal Rabies in Sonoma County, California, 1940-1965*[1]

Year	Total	Domestic			Wildlife		
		Dog	Bo-vine	Other	Skunk	Fox	Other
1940	2	1	...	1 cat ..	.....	...	....
1941	....	...	...	......	.....	...	....
1942	....	...	...	......	.....	...	....
1943	1	...	1	......	.....	...	....
1944	1	...	1	......	.....	...	....
1945	1	...	1	......	.....	...	....
1946	3	...	3	......	.....	...	....
1947	7	...	5	1 horse.	.....	1	....
1948	1	...	1	......	.....	...	....
1949	3	...	2	......	.....	1	....
1950	18	...	...	1 cat...	6	10	1 bobcat..
1951	6	1	3	......	.....	2	....
1952	3	...	2	......	1	...	....
1953	2	...	1	......	.....	1	....
1954	13	1	3	1 horse, 1 sheep	2	3	1 raccoon, 1 bat....
1955	18	2	6	1 cat...	6	3	....
1956	5	1	1	......	3	...	....
1957	3	...	1	......	2	...	....
1958	8	1	2	......	3	2	....
1959	7	...	5	......	1	1	....
1960	9	1	1	......	6	1	....
1961	15	...	5	......	8	1	1 bat.....
1962	23	1	3	......	16	2	1 bat.....
1963	18	...	1	3 horses	12	1	1 bobcat..
1964	8	...	...	......	7	1	....
1965	13	...	5	......	7	...	1 bobcat..

[1]Source: Rabies, California Statistical Report Tables 1922-1965

around the dairy barns prior to the occurrence of rabies in cattle. The case of bat rabies in Sonoma County in 1954 was the first one recognized in bats in California (2). It will be noted that this case of bat rabies occurred at a time when a variety of animals were infected with rabies in Sonoma County. However, rabies in freetail bats, Tadarida brasiliensis, has been occurring in epidemic proportions in this species of bat in the Southwest since 1954, and I believe that the cases of rabies in Tadarida bats in California are unrelated to the endemic foci of the disease in this state. The strains of rabies virus isolated from Tadarida bats are uniformly characterized by a short incubation period for the experimental disease in adult mice and production of numerous Negri bodies, whereas the strains of rabies virus isolated from other bat species are like those obtained from skunks.

Tables 3 and 4 give the statistics on rabies for Glenn and El Dorado counties. Rabies is observed rarely in dogs and other domestic animals in these counties, but wildlife rabies has been known since the days of the Gold Rush. Glenn

Table 3.—*Animal Rabies in Glenn County, California, 1950-1965*

Year	Total	Domestic			Wildlife	
		Dog	Bovine	Other	Skunk	Other
1950..	....	...	......	....	.....	....
1951..	....	...	......	....	.....	....
1952..	....	...	......	....	.....	....
1953..	....	...	......	....	.....	....
1954..	2	1	......	....	1	....
1955..	3	...	......	....	3	....
1956..	3	...	......	....	3	....
1957..	5	...	1	....	[1]4	....
1958..	3	...	......	....	3	....
1959..	2	...	......	....	.....	1 fox, 1 bat
1960..	....	...	......	....	.....	....
1961..	2	...	[2]1	....	1	....
1962..	2	...	2	....	.....	....
1963..	1	...	......	....	.....	1 bat ....
1964..	3	1	......	....	2	....
1965..	1	...	......	....	.....	1 bat ....

[1]One of these was a spotted skunk (M400)
[2]A spotted skunk was killed in daytime in the same pasture about 1 month before the cow developed rabies.
Source: Rabies, California Statistical Report Tables 1922-1965.

Table 4.—*Animal Rabies in El Dorado County, California, 1947-1965*

Year	Total	Domestic		Wildlife	
		Dog	Other	Skunk	Other
1947.............	....	...	....	.....	....
1948.............	....	...	....	.....	....
1949.............	....	...	....	.....	....
1950.............	1	[1]1	....	.....	....
1951.............	....	...	....	.....	....
1952.............	....	...	....	.....	....
1953.............	....	...	....	.....	....
1954.............	4	...	....	3	1 fox
1955.............	11	...	....	11	....
1956.............	2	...	....	2	....
1957.............	10	...	....	[2]10	....
1958.............	7	...	....	7	....
1959.............	....	...	....	.....	....
1960.............	1	...	....	1	....
1961.............	5	...	....	5	....
1962.............	9	...	....	9	....
1963.............	6	...	....	6	....
1964.............	1	...	....	.....	1 bat
1965.............	3	1	....	2	....

[1]This dog died of rabies following a skunk bite.
[2]One of these was striped skunk M1942.
Source: Rabies, California Statistical Report Tables 1922-1965.

County is the source of spotted skunk M400, mentioned previously. This case of rabies occurred in a rural area near the Sacramento River in the Central Valley of California. The brushland along the river is a good environment for skunks because of the abundance of small mammals. Rabies virus was isolated from the brain, submaxillary salivary glands, mammary gland, and kidneys of this skunk. The virus derived from M512, a spotted skunk inoculated intramuscularly with the virus from the kidney tissue suspension of M400, was used as a source of virus for tissue culture studies. A non-neuro-adapted strain of this virus was established from the submaxillary salivary glands of M512 by cultivation of the virus in hamster kidney tissue culture. This virus is used as a type strain for rabies street virus. El Dorado County is the source of M1942, a striped skunk killed on a ranch near Fairplay, September 23, 1957. The Fairplay area is a foothill region of the Sierra Mountains at an elevation of about 2,500 feet, with mixed grassland and forest, some of which is brushland with a large population of rodents.

This rabies virus strain is unusual in that it ordinarily produces an asymptomatic infection in adult mice inoculated intracerebrally and also in adult mice inoculated intramuscularly. The titer of the original salivary gland suspension was $>10^{-6}$ / 0.015 ml when tested in infant mice by the intracerebral route of inoculation. The titer in adult mice was $<10^{-1}$ /0.015 ml. Infant mice infected by intracerebral inoculation ordinarily died on day 16 or 17, but some died as late as 29 days after inoculation and were positive for rabies by the FRA test. One infant mouse inoculated intracerebrally with approximately 100 LD_{50} of the original salivary gland virus sickened on day 15, was paralyzed from day 16 to day 22, and then recovered. When killed on day 32, its brain was positive for rabies by the FRA test. The incubation period in weanling mice was usually 20 days, and one mouse that dies 30 days after inoculation was positive for rabies by the FRA test. Only one of 18 adult mice inoculated intracerebrally with 10 infant mouse LD died of rabies. This mouse was found dead on day 12, and the brain was positive for rabies by the FRA test. I believe that this mouse died as a result of fighting with other male cage mates. Eight of the surviving mice were challenged intracerebrally with 10 LD_{50}' of the M512 strain of street rabies virus at 43 days after the original inoculation, and all were immune. Three of the mice were held for 62 days and then killed. The brains of all three were positive by the FRA test, but the test for virus in infant mice was negative. Adult mice inoculated intramuscularly with 10^4 infant mouse LD_{50} survived 43 days without any signs of illness. They were then challenged with $>10LD_{50}$ of the M512 strain of street rabies virus and were all immune. Mice dying after inoculation with the original salivary gland suspension of the M1942 striped skunk were negative for Negri bodies. This is an example of the type of rabies virus that may be encountered in naturally infected skunks and which would not have been misfound by the diagnostic methods commonly employed for the diagnosis of rabies. The sporadic cases of rabies in Glenn and El Dorado counties are a very good example of endemic wildlife rabies. Here again the skunk is the animal most commonly found infected with rabies, but there is no evidence of a continuing epidemic cycle of the disease in this animal.

Tables 5 and 6 give the statistics for rabies in Los Angeles County and Ventura County. This illustrates the occurrence of dog rabies in a large city with a large population of domestic dogs and an adjacent county with the same natural ecology but with a smaller dog population and a good dog control program. The rabies problem in wildlife in Los Angeles County was not recognized until the dog rabies problem was brought under control. Los Angeles County had its own rabies control program until 1957, when it adopted the rabies control program developed by the California State Department of Public Health. Subsequently, dog rabies was rapidly brought under control. In 1956 there were 24 cases of cattle rabies in Los Angeles County (3). These, as well as the cases in the goat and hog, all occurred at one dairy. There was no evidence of exposure of the animals by rabid dogs, and my own investigation of the outbreak led me to believe that it was derived from a skunk or weasel. The irrigated pasture at the dairy was near a rocky ridge covered with brush, which in this area is normally inhabited by weasels and skunks. The history of dog rabies in Los Angeles is an example of how rabies can be maintained for an indefinite period in a large urban center with many domestic dogs unless a well organized rabies control program is developed and enforced. The statistics for Ventura County show how a well run rabies control program will prevent the occurrence of an epidemic of dog rabies in a region where the disease is endemic in wildlife.

The epidemiologic study of rabies by counties in California shows that the disease is endemic in wildlife in certain areas. It is clear that dogs or wild canines do not maintain the disease in these areas. The striped skunk is a sentinel animal, in that cases of the disease occur in this host more frequently than in other wild animals. Rabies also occurs in epidemic proportions in this species of animal. At longer intervals spotted skunks and weasels are found infected with rabies, but the disease does not occur in epidemic form in these animals. There are sporadic cases of rabies in bobcats, but there is no other information that would make one believe that they are the reservoir host of the disease. There are also sporadic cases of bat rabies in the endemic foci of rabies, but these animals do not seem to be the common denominator of the disease. There were 53 cases of bat rabies in California in 1963, 53 in 1964, and 72 in 1965. The cases in

Table 5.–*Animal Rabies in Los Angeles County, California, 1950-1965*

Year	Total	Domestic				Wildlife		
		Dog	Cat	Bovine	Other	Skunk	Bat	Other
1950.	27	23	4	...	.....	.....	...	....
1951.	24	18	5	...	.....	.....	...	1 gopher.
1952.	93	77	11	1	.....	.....	...	1 gopher, 1 weasel
1953.	142	139	3	...	.....	.....	...	....
1954.	26	25	1	...	.....	.....	...	....
1955.	219	218	1	...	.....	.....	...	....
1956.	131	101	4	24	1 goat, 1 hog	.....	...	....
1957.	26	23	1	...	.....	1	...	1 fox ...
1958.	9	2	1	...	.....	6	...	....
1959.	2	1	...	...	.....	1	...	....
1960.	4	1	...	...	.....	3	...	....
1961.	35	1	...	...	.....	32	1	1 monkey
1962.	7	...	1	...	.....	2	4	....
1963.	7	...	...	...	.....	1	6	....
1964.	70	...	...	2	.....	60	3	4 foxes, 1 raccoon
1965.	22	...	...	...	.....	16	6	....

Source: Rabies, California Statistical Report Tables 1922-1965.

Table 6.–*Animal rabies in Ventura County, California, 1922-1965*

Year	Total	Domestic		Wildlife	
		Dog	Other	Skunk	Other
1950	4	...	....	4	....
1951	4	...	....	4	....
1952	4	...	....	3	1 fox.....
1953	4	4	....	.....	....
1954	1	...	....	1	....
1955	10	...	....	10	....
1956	16	2	....	14	....
1957	15	...	1 cat	11	3 foxes...
1958	9	...	....	9	....
1959	11	...	....	9	1 fox, 1 bat
1960	13	...	....	13	....
1961	11	1	....	10	....
1962	2	...	....	2	....
1963	5	...	....	5	....
1964	9	...	....	8	1 fox.....
1965	9	...	....	9	....

Source: Rabies, California Statistical Report Tables 1922-1965.

Tadarida bats appear to be unrelated to the wildlife rabies foci in California.

The occurrence of sporadic cases of rabies in solitary bats in areas where rabies is active in wildlife suggests that some of the cases of bat rabies are derived from exposure to skunks or other carnivores. The majority of the cases of rabies in the solitary bats Lasionycteris noctivagans and Lasiurus cinereus occur in the fall during the southward migration of these bats. This indicates that some of these cases are derived from exposure in the north of California. In the course of a study of arboviruses in wildlife, a large number of bats have been tested for viruses by the infant mouse test. Rabies virus has been isolated from bats, but in each instance the virus was present in the brain, indicating that the bat had encephalitis.

Rio Bravo virus and Kern Canyon virus have been isolated from apparently healthy bats. In studies of the organ tropism of wildlife viruses we have studied 24 bats naturally infected with rabies. The brain was positive for rabies virus in each case. To test for virus, various organs are taken out with separate sets of sterile instruments and then rinsed several times with sterile saline solution after cutting into the tissue. This is done to eliminate the blood, which may contain antibodies. The specificity of each rabies virus isolation is checked by the FRA test. Lung tissue from 17 of the rabid bats was tested and of these 8 (47 percent) were positive for rabies virus. The pectoral muscle was tested on 14 of the bats, and 8 (57 percent) were positive. Ten of 20 submaxillary salivary gland specimens (50 percent) were positive. Only 2 of 19 kidney specimens (10 percent) were positive for rabies virus. In three instances the lung tissue was positive for rabies virus and the submaxillary salivary glands were negative.

In surveys for arboviruses, the pharynx, trachea, submaxillary salivary glands, and lungs are pooled in the test for virus. In four instances this pool was tested before it was known that the bat was positive for rabies. In each instance the rabies virus was obtained from the pool of the upper respiratory tract tissues. In one of these bats the blood was obtained for study by mincing the heart and lungs in the diluent. Rabies virus was isolated from this bloody fluid. There was enough virus in the fluid released from the lung tissue to infect the mice, although the alveolar fluid was diluted $>10^{-2}$. This makes it clear that a mouth swab may contain rabies virus while the submaxillary salivary glands are negative for virus. Of course, the virus may also be derived from the lachrymal glands

Studies of rabies virus derived from naturally infected skunks show that the virus has a tropism for certain organs such as the brain, salivary glands, lungs, pancreas, mammary glands, kidneys, and muscle tissue. The highest titers of virus have been obtained from the submaxillary salivary glands. The brain tissue of naturally infected skunks usually has a titer of $<10^{-3}$, and in some there appears to be little active virus. This serves to explain why these animals are relatively alert and physically strong during the early stages of the disease. We have recently isolated rabies virus from the pectoral muscle and the intestinal mucosa of a naturally infected skunk. This striped skunk M2079 was killed when found wandering about in daytime at the Hopland Field Station of the University of California in Mendocino County on March 26, 1965. The brain, submaxillary salivary glands, parotid salivary glands, lungs, and kidneys were also positive for rabies virus. The liver, spleen, pancreas, lymph node pool, thigh muscle, scent gland, and intestinal contents were negative for virus. The lung tissue appeared entirely normal, and the specimens tested were taken from the periphery of the lungs.

Rabies virus appears to be a member of the myxovirus group, and the tropism of the virus for the respiratory tract is in line with what one would expect for a member of this group of viruses. In searching for the virus in wildlife, it is evident that we should test tissues of the respiratory tract, especially the salivary glands and lungs. It would also be advisable to test the nasopharynx, pharynx, and trachea so as to include the entire respiratory tract. The infant mouse appears to be the best test animal. The epidemiological studies reported in this paper show that rabies is maintained in certain regions of California in wildlife. It is such areas that should be studied over a period of years to learn more about the reservoir host or hosts of rabies virus in wildlife. Each year we learn about an occasional instance of a weasel's attacking persons in daytime or of this animal's acting tame. This type of behavior makes one believe that the animal is probably rabid; however, weasles have seldom been found positive for rabies in California.

The tests employed for diagnosis would ordinarily have failed to reveal the peculiar strains of rabies virus now known to occur in skunks and bats. The FRA test will be particularly important in the diagnosis of rabies in wildlife hosts such as skunks and weasels. Weasels are present in all the known foci of endemic rabies in North America. In other words, this animal is the common denominator of the disease as regards known wildlife hosts of rabies. On the basis of our knowledge of the epidemiology of parasitic diseases of wildlife, we would not expect to observe epidemics of rabies in the longterm natural wildlife host of rabies virus.

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Wolf, Fox, and Coyote Rabies

R. Keith Sikes, D.V.M.[1]

Although the dog is the most important single vector of human rabies, various wildlife species are also major sources of infection. Several wild members of the Canidae family are especially important vectors of the disease. In this paper, I will summarize available information about rabies in three of the wild members of this family that are found in the United States: wolf, fox, and coyote.

Wolf Rabies. According to a recent WHO report (8) the wolf is an important reservoir or vector of rabies in 10 countries—Afghanistan, Greece, India (Hassar), Iran, Iraq, Jordan, Mongolia, Turkey, UAR-Egypt, and Yugoslavia. Iran and other countries of the Eastern Mediterranean area have had severe problems with rabies in wolves. Between 1950 and 1965, 58 human rabies deaths occurred among 424 people bitten by rabid wolves in Iran. In Russia, from 1957 to 1963, four deaths occurred among 92 people bitten by rabid wolves. Between 1961 and 1963, Turkey reported six human deaths from rabies as a result of wolf bites, Yugoslavia reported two, and Italy one.

A rabid wolf is a very vicious and strong animal, capable of inflicting severe injuries. It is not uncommon for a single rabid wolf to bite 10 or more people. One such incident which occurred in Iran in 1954 was utilized by members of the WHO Expert Rabies Committee to demonstrate the efficacy of passive immunization in antirabies therapy (1). On this occasion 29 persons were bitten by a rabid wolf during a 5-hour period at night. Seventeen of them were bitten on the head and 12 on the trunk and limbs only. The most severe exposure was sustained by a 6-year-old boy who was bitten through the cranium. Various regimens of antirabies serum and/or vaccine were administered to these people. As a result of this field trial, and additional laboratory studies, antirabies serum is widely used in post-exposure treatments today.

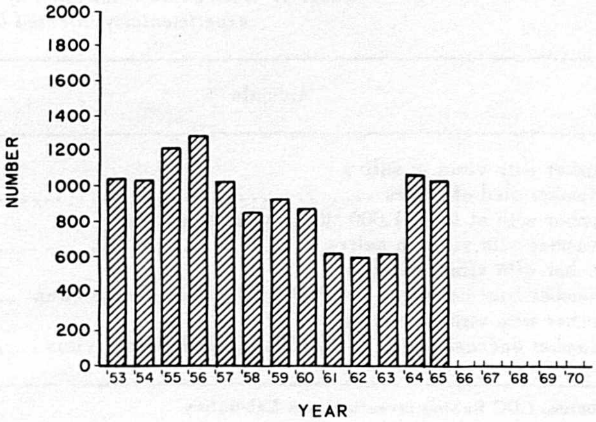
Two species of wolves (Canis lupus, the gray wolf, and Canis niger, the red wolf) are found in the United States, but they do not constitute a serious rabies problem, probably because they are not present in sufficient numbers for the infection to become established in them. During the past 10 years, five states, Alaska, Arkansas, Missouri, Louisiana, and Texas, have reported a total of 15 laboratory-confirmed cases of wolf rabies.

Fox Rabies. Foxes are reservoirs or vectors of rabies in 14 countries—Canada, Czechoslovakia, Denmark-Greenland, Germany (Fed. Republic), India (Assam), Iraq, Jordan, Lebanon, Mongolia, Portugal, Turkey, UAR-Egypt, United States, and Yugosalvia. In the 1962-1963 World Survey of Rabies (8), foxes were listed as the second most commonly infected wild animals. Jackals were the most widely infected wild animals in the world, with 26 countries reporting them as either reservoirs or vectors of rabies infection.

In North America, rabies is known to have been epizootic in foxes in Massachusetts during the first decade of the 18th century (6), in Alabama in 1890 (7), and in Alaska in 1915 (3). Since 1940, rabies has become prevalent in foxes in the eastern and southern United States. The annual incidence of laboratory-confirmed fox rabies in the United States since 1953 is shown in Figure 1. In the United States, six human rabies deaths have been attributed to the bites of rabid foxes during the past 20 years.

Most of the fox rabies is found in the Appalachian Mountain area and the Gulf Coast states.

Figure 1.–*Cases of rabies in foxes*



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Throughout these areas, the red fox (Vulpes fulva) and the grey fox (Urocyon cinereoargenteus) are common. The Arctic fox (Alopex logopus) is found in Alaska and is the principal reservoir of rabies infection there.

Foxes have been shown to be extremely susceptible to rabies virus when challenged with viruses isolated from the salivary glands of foxes or skunks (3, 2) or when exposed to aerosol infections in bat caves (2). In a series of studies comparing susceptibility among various wildlife species, the fox was shown to be the most susceptible (Table 1).

Table 1.—*Calculated doses of an isolant of street rabies virus necessary to kill 50 percent of various species of wild animals inoculated peripherally*

	Foxes	Skunks	Raccoons	Opossums
Number of MLD_{50}	<5	500	1,000	>80,000

An interesting phenomenon concerning the relationship between inoculum and the amount of virus recovered from the saliva (Tables 2, 3) has been observed in experimentally infected foxes (5). Foxes inoculated with more than 10^3 mouse LD_{50} of rabies virus had short incubation periods—all less than 18 days. Generally, this was too short a time for the virus to become established in the salivary glands, and no virus was detected in their saliva. Foxes inoculated with less than 10^3 mouse LD_{50} of rabies virus had longer incubation periods—usually 38 days or longer—and almost all emitted virus in their saliva. The saliva of some titered 10^3 or greater, high enough to infect skunks.

From this data, it seems probable that areas which experience only fox rabies for several years might expect an eventual "spill-over" of infection into skunks. This seems to have been the case in

Table 2.—*Comparative results of inoculation of street rabies virus in foxes and skunks*

Inoculum (MLD_{50})	Rabies deaths	Incubation period (days)		Period of clinical illness (days)	
	Number inoculated	Range	Median	Range	Median
Foxes:					
14,000	6/7	12-17	13	1-3	1.5
1,400	7/7	15-18	16	1-2	1.0
140	[1]4/5	16-24	20	1-3	2.0
14	7/7	23-109	56	1-3	2.0
Total	24/26	.....	..	.....	.....
Skunks:					
140,000	7/7	17-78	22	1-6	1.0
14,000	6/6	14-20	19	2-13	5.5
1,400	5/6	17-88	76	1-5	2.0
140	[1]0/4	.....	..	.....	.....
Total	18/23	.....	..	.....	.....

[1]Excluding 2 deaths from other causes.
Source: CDC Rabies Investigations Laboratory.

Tennessee and Texas. In both states, fox rabies was recognized and reported as a rabies problem in 1946. Since that time, Tennessee has experienced a general increase in fox rabies; 799 laboratory-confirmed fox rabies cases have been reported in the last 2 years. Subsequent to the increase in fox rabies in Tennessee, there has been a marked increase of skunk rabies. A total of 102 rabid skunks have been reported from Tennessee in the past 2 years; in the previous 11 years, only 72 skunk rabies cases were reported. In Texas, fox rabies was more prevalent during the years 1953-1959, but from 1960 through 1965, skunk rabies has been more prevalent.

Coyote Rabies. Coyotes are the small, brush wolves that appear only in North America—

Table 3.—*Data on demonstration of rabies virus in saliva of wild animals experimentally infected by the intramuscular route*

Animals	Foxes	Skunks	Raccoons	Opossums
Number with virus in saliva / Number died of rabies	10/24 (41%)	15/18 (83%)	7/11 (63%)	0
Number with at least 1,000 MLD_{50} virus in saliva / Number with virus in saliva	2/10 (20%)	11/15 (73%)	2/7 (28%)	0
Number with virus in saliva / Number succumbing to >10,000 MLD_{50} of challenge virus	1/6 (16%)	11/13 (84%)	3/5 (60%)	0
Number with virus in saliva / Number succumbing to <1,000 MLD_{50} of challenge virus	8/11 (73%)	0	1/2 (50%)	....

Source: CDC Rabies Investigations Laboratory primarily in the west. They are apparently extremely susceptible to rabies, since they die as readily as foxes do when exposed to aerosol rabies infection (2).

Coyote rabies was quite a serious problem in some of the western states more than 30 years ago. However, during the past 10 years, a total of only 58 rabid coyotes have been reported in the United States and, although they are a potential hazard as a reservoir or vector of rabies, they do not appear to be of major epidemiologic significance at the present time.

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Rodent Rabies

William G. Winkler, D.V.M.[1]

Although it is not correct from a strictly taxonomic viewpoint, I would like to include in this discussion of rodent rabies not only rodents, but also the closely related lagomorphs, rabbits and hares, as well as rodents in the strictest sense.

While it has been impossible to obtain accurate data regarding the species of animals responsible for inflicting bite wounds on man, I believe that second only to the domestic dog, the rodent group is responsible for more bites than any other category or species. By the same token, it is probable that second only to domestic dogs, rodents are responsible for more human antirabies treatment than any other species or category. Herein lies the importance of rodents in rabies, not in their potential as vectors or reservoirs, but in the number of non-rabid rodents that bite man, resulting in the administration of unnecessary and unwarranted antirabies treatment.

Overtreatment administered for rodent bites results from a combination of several factors including (1) epidemiology of rodent bites, (2) criteria established for recommending treatment, and (3) laboratory misdiagnosis.

Consider the epidemiology of rodent bites for a moment: squirrels and rats, the two most important rodent species, thrive in close cohabitation with man. Population densities and contact rates are high, particularly in urban areas. They are accustomed to the presence of man and are not so shy and retiring as most of our truly wild animals. To compound the exposure rate, man and his children train squirrels to take food from the hand, inevitably resulting in more bites. The likelihood then of a normal, non-rabid rodent biting man is infinitely greater than the likelihood of a normal, non-rabid skunk, fox, wolf, etc., biting man.

Regarding treatment criteria, a disproportionately high percentage of biting rodents escape and are thus not available for observation or laboratory examination. A bite inflicted by an escaped wild animal may technically be considered a severe exposure, and many are treated as such.

Even with those rodents that do get to the laboratory, we find treatment advocated where it may not be indicated. We are all aware of the "non-specific" inclusion bodies sometimes found in rodents. Laboratories have been known to confuse these inclusion bodies with the Negri body of rabies and recommend treatment on this basis. The advent of fluorescent antibody diagnosis and its acceptance by diagnostic laboratories has probably reduced the number of human treatments resulting from this misdiagnosis.

I mentioned that statistics were not available on the species responsible for human bite injuries. However, there is data available which may be substituted for this information. That is, the data compiled by state health department laboratories on species submitted for rabies examination. I have a few figures which, though far from complete, are probably representative of the national picture.

If we average all of the figures cited in Tables 1 through 4 we find that for a total of 35 state-years, rodents account for 25 percent of all heads examined, dogs for 35 percent, and other species 40 percent.

Table 5 shows the breakdown of rabies-positive heads for the past decade. If these figures are compared with the percent of heads examined (Tables 1-4), we see that although rodents account for 25 percent of submissions they represent less than 0.5 percent of positives; dogs account for 35 percent of submissions and 24 percent of positives; and other species account for 45 percent of submissions and 75 percent of the positives.

It is interesting to note the considerable disparity in infection rates of the several species. There are a number of possible explanations: (1) the criteria used to determine which individuals shall be examined may vary with the species, (2) there may be other diseases, particularly in rodents, which clinically "mimic" rabies, (3) rodents may be easier to submit for examination than larger species, and so on.

Additional data relating to rodent rabies is seen in Tables 6 through 8. From the data in Table 6 it appears that the squirrel is the most important rodent so far as potential human rabies exposure is concerned. Again though, it is neces-

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sary to remember that non-specific inclusion bodies are frequently found in squirrels, and these may be confused with Negri bodies on direct microscopic examination.

Table 1.–*Rodents and other species examined for rabies in one Eastern State–five-year period*[1]
[No positive rodents, seven other animals positive]

Species	Number Examined	Percent
Squirrel	166	9.5
Other rodent	349	19.8
Total rodent	515	29.3
Dog	603	34.4
All others	638	36.3
Total	1,756	100.0

[1]New Jersey–1953, 1956, 1957, 1958, 1961

Table 2.–*Rodent and other species examined for rabies in one Eastern State–twenty-year period*[1]
[Two positive rodents, 5,210 positive other animals]

Species	Number Examined	Percent
Squirrel	1,231	4.0
Other rodent	1,522	5.0
Total rodent	2,753	9.0
Dog	13,161	46.0
All others	12,731	45.0
Total	28,645	100.0

[1]Georgia 1946-1965

Table 3.–*Rodents and other species examined for rabies in one Western State–two-year period*[1]
[No positive rodents, 550 positive other animals]

Species	Number Examined	Percent
Squirrel	122	2.0
Other rodent	2,316	40.0
Total rodent	2,438	42.0
Dog	920	16.0
All others	2,497	42.0
Total	5,855	100.0

[1]California–1964-1965

Table 4.–*Rodents and other species examined for rabies in one Eastern State–eight-year period*[1]
[One positive rodent, 564 positive other animals]

Species	Number Examined	Percent
Squirrel	2,516	12.0
Other rodent	3,964	18.0
Total rodent	6,480	30.0
Dog	6,316	30.0
All others	8,354	40.0
Total	21,150	100.0

[1]Florida–1957-1965

Table 5.–*Rabies in rodents and other species United States–1956-1965*

Species	Number	Percent
Squirrel	74	.2
Other rodent	125	.3
Dog	10,363	23.8
All other	32,900	75.7
Total	43,462	100.0

Table 6.–*Reported laboratory confirmed cases of rabies in rodents for 10-year period United States–1956-1965*

Animal	Number	Animal	Number
Guinea pig	2	Muskrat	21
Hamster	5	Woodchuck and groundhog	34
Mouse	18	Prairie dog	1
Rat	19	Porcupine	1
Squirrel	74	Beaver	3
Flying squirrel	1	Rabbit	1
Chipmunk	8		
Gopher	11	Total	199

The rather sharp reduction in laboratory-diagnosed rodent rabies cases in the last half of the decade (1956-1965) is shown in Table 7. A plausible explanation may be the improved diagnostic capabilities of laboratories since the development of fluorescent microscopy.

The most telling evidence of the unimportance of rodents in the transmission of rabies to man is seen in Table 8. There has not been a

Table 7.—*Rabies in rodents and other species United States— 1956-1965*

Years	Rodents	Total Animals	Percent Rodents
1956-1960................	128	22,972	0.56
1961-1965................	71	20,490	0.35
Total................	199	43,462	

NOTE: In the two periods shown, there is an 11% decrease in total rabies and a 43% decrease in rodent rabies in second half of the decade.

Table 8.—*Species responsible for human rabies death United States – 1946-1965*

Years	Dog	Fox	Bat	Skunk	Cat	Unknown[1]	Total
1946-1955....	82	3	1	4	4	26	120
1956-1965....	19	3	2	2	2	[2]10	38
20-yr total.	101	6	3	6	6	36	158

[1]Many unknowns are presumably dog origin based on unconfirmed history.

[2]Includes two (2) cases later presumed to be the result of aerosol transmission in bat cave.

single case of rodent origin human rabies in this country for at least 20 years.

Experimental data generally indicate that most rodents are not particularly susceptible to rabies infection, and even when they are infected, the virus does not usually invade salivary glands.

In summary, I believe that under field conditions, rodent rabies is a relatively rare phenomenon. The potential hazards still a part of antirabies treatment in most cases outweigh the risk of rabies infection resulting from a rodent bite. More critical evaluation of rodent specimens submitted for rabies examinations, particularly salivary gland testing, may shed light on how much significance we should attach to rodent bites.

Rabies in Northern Greenland: Some Observations on the Epizootiology and Etiology

Robert A. Crandell, Lt.Col., V.C., USAF[1]

Rabies is distributed over vast land areas above the Arctic Circle in both the Eastern and Western Hemispheres. Epizootics of a rabies-like disease have been known to occur among the sled dogs of northern Greenland and Alaska for nearly a century. A similar condition known as "rabidity" has occurred for many years in the Arctic foxes and other animals in the polar regions of Russia. Although epidemics among sled dogs in the Canadian Arctic were first described in the 1930's the history of rabies in the Northwest Territory probably dates back to the late 19th century. Rabies infections in the animals of these areas have been referred to by many names, including Arctic dog disease, rabidity, polar madness, Arctic nervous disease, and fits.

The etiology, epizootiology, and control of rabies in these areas have been studied extensively only during the past two decades. In 1947, Plummer (14, 15) demonstrated that rabies virus was present in the wildlife of three widely separated areas of the Northwest Territories. Williams (18) established the fact that rabies was widespread in Alaska and that it reached epizootic proportions in 1945-47. The comprehensive paper by Rausch (16) on rabies in Alaska and in other high boreal regions is recommended for those interested in the natural history of rabies in wild canids. During the years 1954-62, Kantorovich (8, 10) studied the disease in the polar area of Russia and clearly showed the cause to be rabies virus.

Wamberg (17) recently reviewed the literature describing the condition as it had existed in Greenland and reported four recent epizootics in dogs in western Greenland. These epizootics occurred in the Upernaviks district in 1956-58, in the Thule district in 1958-59, the Umanak district in 1959, and in the Egedesminde district in 1959-60. During the last named epizootic more than 1,000 dogs were reported to have died (11). Rabies was first reported in a sled dog from the east coast of Greenland in 1963.

The U.S. Air Force became interested in the rabies problem in northwest Greenland in 1959. In June of that year the Danish Government requested assistance in studying a rabies-like disease among sled dogs and Arctic foxes. An epizootic in the southern Thule district of a disease called "fits" became so severe that during the winter of 1958-59, 50 percent of the dogs died. The very existence of native Greenlanders, who depend on the sled dog and Arctic fox, was threatened. This outbreak created economic and health problems for the natives and certainly was a potential health hazard for American servicemen stationed in that area.

Although the disease had been recorded as existing in Greenland for more than 100 years, its true nature was unknown. Rabies had been suspected but never proven. Despite recurrent outbreaks among dogs, no human cases had been reported from Greenland, where adults and children in particular are often attacked and severely bitten by aggressive dogs. The first proven case of human rabies occurred in 1960 in a 4-year-old Greenlander girl (11).

The diagnosis of rabies in animals from Greenland was first verified in June 1959 by the Communicable Disease Center at their Montgomery Laboratories in Alabama in one fox and one dog (6). Later, the State Veterinary Serum Laboratory in Denmark confirmed the diagnosis in six out of seven dogs (17).

The purpose of this paper is to summarize available laboratory data concerning rabies in northwest Greenland during the 5 post-epizootic years 1961-65, to note some factors which influence the epizootiology of the disease, and to discuss similarities and differences of the disease in other Arctic regions. The author made one visit to Greenland in 1963 and, with the assistance of the Air Force veterinarians stationed in Thule and of Dr. Kjeld Wamberg, was able to carry out this work on animal heads shipped frozen by air from Thule Air Force Base to the USAF Epidemiological Laboratory in Texas.

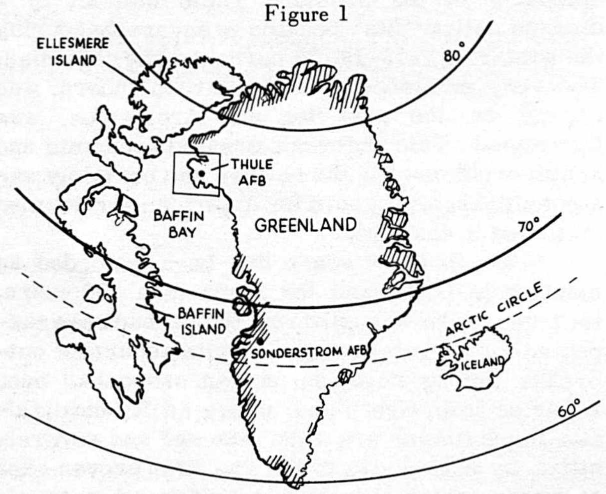
[1] USAF Aerospace, Medical Division, Lackland AFB, Texas.

EPIZOOTIOLOGY

In discussing the epizootiological aspects of this disease in Greenland, consideration must be given to the relationships between the environment, the etiologic agent, the vector, and the host.

Geographical and Climatic Features: Greenland is the world's largest island and the biggest land mass within the Arctic Circle. The northwestern shore lies 10 miles east of the northernmost point of Canada. It extends from 60° latitude northward slightly beyond 80° latitude. Most of the island lies between 20° and 60° west longitude. Greenland has an inland plateau surrounded by a fringe of mountains. It is about one-fourth the size of the United States. Of the island's 840,005 square miles, 727,360 are covered by snow. The remainder lies along the cost and is free of ice (Figure 1).

Figure 1



Thule AFB is located 695 miles above the Arctic Circle along the shores of North Star Bay. Temperatures in this area have been as low as 43° F below zero in winter and reach a high of 63° F above zero in the summer months. The average annual temperatures at Thule range from 20° F below to 45° F above zero, and the average annual snowfall is 30 inches, but additional snow is blown in off the polar cap.

Beginning in November. the sun remains below the horizon for 3 months. Following the dark season, the sun returns and stays in the sky longer each day until early summer. During the 3 months of summer, the sun remains above the horizon 24 hours a day.

Because of the distances, terrain, and lack of roads, transportation in the area is restricted. Land transportation is limited to dog teams in the winter. The sea is open during the summer and allows access to coastal villages. Air travel to the remote areas in the north is possible by helicopter.

Land Mammals: In addition to sled dogs, reindeer (caribou), Arctic foxes, Arctic hares, wolves, polar bears, and musk-ox are the chief land mammals found in Northern Greenland. Sled dogs are found in each village, and in some villages there are more dogs than people.

ETIOLOGIC AGENT

Isolation and Identification. All laboratory diagnoses on animals sent from Greenland to the USAF Epidemiological Laboratory were made by the fluorescent antibody technic and confirmed by virus isolation in mice. Isolated viruses were identified by serum neutralization test. The number of animals tested and found positive is shown in Table 1. A total of 94 animals were examined for rabies, and 32 (34 percent) were positive. Of the 60 dogs studied, 16 (22.9 percent) were positive, and 16 of the 34 foxes (47.1 percent) were found to be infected with rabies virus. The fluorescent antibody technic and mouse inoculation method for diagnosis were shown to be equally sensitive. A more detailed account of the isolation procedures is published in a previous report (2) (Figures 2-4).

Table 1.–*Number of Arctic foxes and sled dogs examined and found positive for rabies 1961-1965*

Year	Dogs			Foxes			Totals		
	Tested	Number Positive	Percent Positive	Tested	Number Positive	Percent Positive	Animals Tested	Animals Positive	Percent Positive
1961	4	2	50.0	18	10	55.5	22	12	54.5
1962	4	1	25.0	1	0	0.0	5	1	20.0
1963	33	7	20.3	9	1	11.0	42	8	19.0
1964	17	6	35.2	3	2	40.0	20	8	40.0
1965	2	0	0.0	3	3	100.0	5	3	60.0
Total	60	16	22.9	34	16	47.1	94	32	34.0

Figure 2.–*Monthly distribution of 60 dog and 34 fox heads submitted to the laboratory 1961-1965*

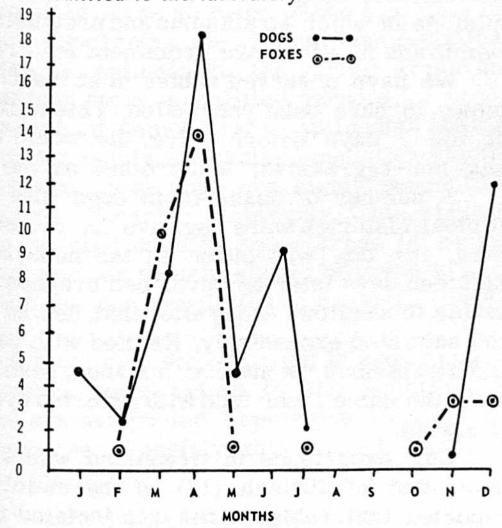


Figure 3.–*Monthly distribution of rabies in dogs and foxes (1961-1965)*

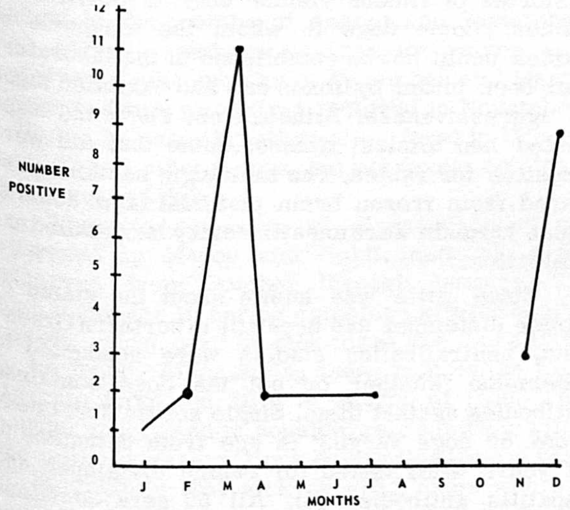
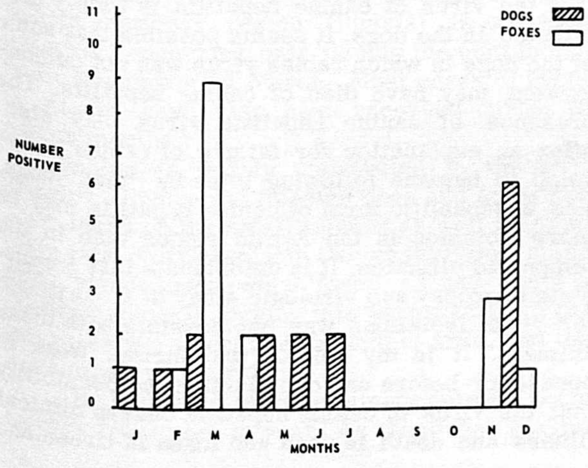


Figure 4.–*Monthly distribution of rabies in dogs and foxes (1961-1965)*



Properties. Negri bodies were not demonstrated in Seller's stained brain impression smears made from these positive animals. The absence of Negri bodies is a feature of rabies infection in the Arctic regions. Kantorovich (8), in his original work, observed that inclusions were found more rarely in polar madness than in typical rabies. Rausch (16) reported that routine microscopic examinations were not made in their study because it had been noted that typical Negri bodies are usually not visible in rabid animals in Alaska. More recently, cytoplasmic inclusion bodies typical of Negri bodies were found for the first time in Arctic foxes of the far north of Russia (10).

Crandell (2) demonstrated cytoplasmic inclusion bodies in the brains of mice, hamsters, and guinea pigs inoculated with different virus isolates from foxes. These occurred in various sizes and shapes with and without internal structure. In addition to the cytoplasmic inclusions, intranuclear inclusions were demonstrated in some laboratory infected animals. This same observation had also been made by Kantorovich (8) in his earlier work.

The Arctic isolates were shown to be infective for rabbits, guinea pigs, white mice, and hamsters by different routes of inoculation (2). The hamster was found to be more susceptible than white mice for primary isolation.

The virus has been shown to be sensitive to treatment with ether (3).

An Arctic strain was compared serologically by cross neutralization tests with fixed virus (CVS) and with viruses isolated from a bat and a cat. The constant virus-serum dilution method was used. Following incubation at 37°F for 90 minutes 0.03 ml of each serum-virus mixture was inoculated into five 3-week-old white mice. The results are given in Table 2.

Table 2.–*Results of cross neutralization tests with four strains of rabies virus*

Virus Strain	Number of MLD_{50}	Neutralization Titer			
		Antisera			
		CVS	Arctic	Street	Bat
CVS	21	1,390	331	316	300
Arctic	5	817	1,390	116	75
Street	17	328	174	225	59
Bat	15	488	126	54	790

These results suggest dissimilarity among the viruses studied. Since the sera prepared against the CVS and Arctic viruses showed serum potency, their results appear to support the existence of antigenic differences. Results obtained with the lower titer sera of the street and bat rabies are of questionable value; however, both of these viruses when tested with the sera of the CVS and Arctic viruses gave titers of lower magnitude than with the homologous systems. In replicate titrations, difficulties were encountered in reproducing some of the reported serum titers. Possible explanations for these discrepancies may be in the low reliability of the rabies neutralization system. Since the Arctic, street, and bat rabies viruses were not fully adapted to mice, it was difficult to repeat virus titrations with reproducible infectivity titers. The size of the Negri bodies of these viruses all differed, so that the "antigenic mass" may have influenced the neutralization capacity of the viruses. The number of test animals used per dilution was too small for firm comparisons.

These weaknesses indicate that further work is necessary before strong positive statements regarding the interrelationship of these viruses can be made. However, since antigenic differences have been shown to exist between fixed viruses (5), between vampire bat virus and fixed virus (7), and between fixed and street virus (12), it is reasonable to postulate that these northern strains have undergone similar changes. This seems particularly reasonable when one considers the varied animal hosts and environmental conditions in which the viruses have been perpetuated in nature.

THE DISEASE IN DOGS

Symptoms in dogs suggest involvement of the central nervous system. Most canine cases are associated with bites from foxes. The incubation period, from contact to appearance of symptoms, has been observed to be as short as 4 days and as long as 14 days. This variation in incubation period is of special interest, because Plummer (13) states that the incubation period is 4 to 5 days whereas Rausch (16) reports it as 2 to 3 weeks. Kantorovich et al. (10), observed a 10 to 12 day incubation period in polar foxes inoculated experimentally in the masseter muscle. Some of the reported cases with seemingly long incubation periods may have been from contact with infected teammates rather than from common exposure. Once the dogs exhibit symptoms, death comes rapidly. The early detectable signs of illness are tremors and profuse salivation with frothing at the mouth. Vomition has been reported in some positive cases. In some animals there is a definite change in the sound of the voice. Snapping at imaginary objects is not uncommon, and many dogs become aggressive. They are unable to swallow food and water. Some animals' hindquarters become paralyzed, and they walk with considerable lack of coordination. Paresis progresses, and the dogs go into coma and die.

Although death is quite often sudden, without convulsions, some animals succumb during convulsions in which strabismus and protrusion of the membrana nictitans are prominent features.

We have observed rabies in at least one dog known to have been vaccinated. This animal was ill for 2 days before dying. He would not eat, was non-aggressive, and frothed at the mouth.

A number of heads from dogs with similar clinical histories were negative for rabies. In one case, the dog was bitten on the nose by a fox. Eighteen days later he developed dyspnea and was unable to swallow. A day after that, he was vicious and salivated excessively. He died with paralysis and strabismus. In another instance, several dogs from the same litter died with reported symptoms of rabies.

Our experience in Greenland was different from that of Rausch (16) on the mainland. He reported that rabies virus was isolated from all canine animals showing aggressive behavior except one coyote from southern Alaska. Our examination of more than 30 heads from animals with histories of illness yielded only 16 positive for rabies. Some dogs in whom the diagnosis of rabies could not be established in the laboratory had been bitten by foxes and had exhibited signs of aggressiveness. Although not all of the foxes tested had clinical illness, some that did were negative for rabies. The histologic sections prepared from frozen brain material from some of these animals were unsatisfactory for detailed examination.

Since little was known about the status of canine distemper and hepatitis in northern Greenland, neutralization studies were conducted to determine whether or not the dogs contained antibodies against them. Single serum specimens from 50 dogs varying in age from 6 months to 11 years were tested for canine distemper and hepatitis antibodies (4). All 50 sera contained significant levels of antibodies against canine hepatitis, whereas no antibodies against the canine distemper virus were detected. These data suggest that the virus of canine hepatitis is widely distributed in the dogs. It seems possible that some of the dogs in which rabies virus was not demonstrated may have died of canine hepatitis. The presence of canine hepatitis virus may also offer an explanation for failure of rabies to develop in humans following bites by "mad" dogs. The encephalitic form of canine hepatitis may be more common in the Arctic region than in the temperate climates. It is unfortunate that a complete necropsy and virologic study of fresh tissue for virus isolations was not possible with these animals. It is my opinion that further work is necessary before one can dismiss the possibility that the virus of canine hepatitis causes clinical illness and death in dogs and foxes in Greenland

and that canine hepatitis is being confused clinically with rabies. I would like to emphasize this latter point because so much of the available information concerning the clinical manifestations of illness in animals in the Arctic areas has been obtained from unqualified persons.

Absence of demonstrable antibodies against canine distemper in the canine population studied suggests that these dogs are highly susceptible to the virus of canine distemper. This virus is enzootic in sled dogs in some areas of Alaska (16), and serious thought should be given to protection of the dog population in northern Greenland.

Sera from nine dogs varying in age from 1 to 6-1/2 years were tested by the agglutination reaction against pooled Leptospira antigens and were negative. Possibly this aspect should be explored further.

SEASONAL OCCURRENCE, DISTRIBUTION, AND INCIDENCE

During this study, heads from sick animals were received for examination throughout the year except in the months of August and September. The highest numbers positive for rabies were received in the months of December and March. Cases in foxes were first received in November, followed by cases in both dogs and foxes in December. Cases among dogs, but not foxes, continued into June and July.

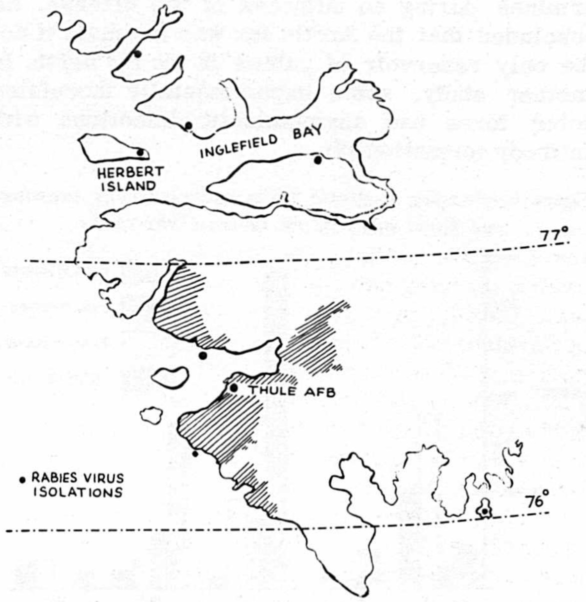
The preponderance of diseased foxes was observed in March and April, and only a few occurred from October through January. The high incidence in spring coincides with the hunting season, when dead or sick foxes are more likely to be found. Also, during these months the foxes migrate from the hills in search of food. They wander freely and in considerable numbers within the military reservations during this time of year. It is unlikely that sick or dead foxes would be seen during the summer in this part of Greenland because they retreat to the mountains for breeding and for summer feeding.

Kantorovich (10) reported that rabidity in the Nenets national region (Russia) is markedly seasonal, occurring only during the cold months from November to March. Most cases of rabies in Alaska have also been recorded during the colder months.

Rabies is widely distributed in the Thule district (Figure 5). Infected dogs and foxes have been found on the small islands as well as on the main island of Greenland. During the recent epizootic, rabid foxes were found as far south as Sondrestrom AB. During this period of study only two foxes were received from that area, and they were negative for rabies.

The incidence of rabies among animals seems to vary from year to year. As mentioned earlier,

Figure 5.—*Distribution of rabies in Northwest Greenland*



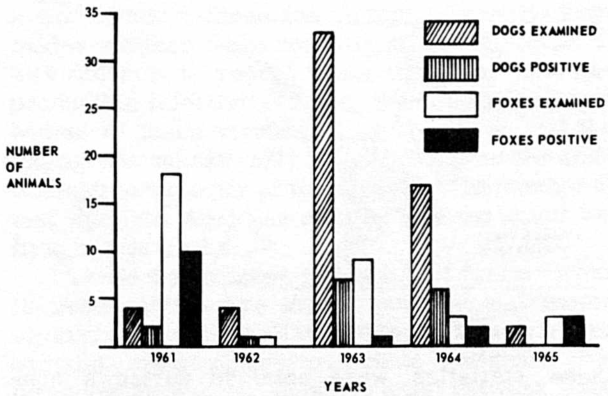
these statistics were obtained during a non-epizootic period and do not necessarily reflect the true incidence of disease. Although unknown ecological factors no doubt contribute to the cause of epizootics, Kantorovich (10), Plummer (13), and Rausch (16) have related severe outbreaks during years of high population density of foxes. Kantorovich (10) has also correlated sudden outbreaks with marked migration of animals.

VECTORS AND RESERVOIRS

There is no question that the Arctic fox is the vector for transmitting rabies virus to sled dogs. I do not know whether the fox is the main or only reservoir in Greenland. To my knowledge, only dogs and foxes have recently been examined for rabies. During my 5 years of association with this problem, unusual deaths in other species have not been brought to my attention.

In Canada a number of wild mammals (bears, beavers, caribous, coyotes, foxes, lynxes, moose, mice, rabbits, wolves, and weasels presumed to be Mustaela erminea) have been found to be infected with rabies. Rabies has been demonstrated in red foxes, Arctic foxes, and wolves in Alaska. In the far north of Russia, rabies virus was isolated from polar foxes, wolves, dogs, foxes, and deer. In considering the fox as the main reservoir for the rabies virus, it is of particular interest to note that Kantorovich (10) reported extremely high virus isolation rates from seemingly healthy Arctic foxes. The percentage of "carriers" among healthy Arctic foxes ranged from 69 to 75 percent during epizootics to 3 to 10 percent during inter-epizootic periods. This same author reported negative results in isolation attempts from healthy animals, including 52 owls, 2,835 murine rodents, and 15 ermines during an outbreak of the disease. He concluded that the Arctic fox was the main if not the only reservoir of rabies in the far north. In another study, some experimentally inoculated polar foxes had asymptomatic infections with antibody formation (9).

Figure 6.–*Number of Arctic foxes and sled dogs examined and found positive for rabies (1961-1965)*



In this regard, we had the opportunity of testing a fox found playing with a litter of puppies. The fox showed no apparent illness but was shot. Rabies virus was isolated from both the brain and salivary gland of this animal. Since the fox is a highly susceptible animal to rabies in the United States, one would not expect these infected animals to live long enough to be the reservoir host. However, with the mixing and migration of such infected animals it is likely that during periods of high population density they could act as the foci of infection. It is interesting to note that in the 5-year period of this study no rabies-positive foxes were submitted to the laboratory in 1962. During that year, rabies was confirmed in only one dog.

SUMMARY

Known characteristics of rabies viruses isolated from animals in the Arctic are reviewed. Rabies is enzootic in the fox population of northwest Greenland and appears in sled dogs when foxes begin their fall migration. Evidence is presented to support the hypothesis that other agents, in addition to rabies virus, are responsible for some clinical illnesses seen in dogs and foxes in the area studied. Additional studies are required to determine the exact nature and cause of these illnesses and to define the reservoir host or hosts of rabies.

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RABIES CONTROL IN THE UNITED STATES

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Canine Rabies Vaccines

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Nervous Tissue Vaccines. "The antecedent cause of the disease (in man) is the bite of a mad dog or, as many say, of other animals, such as the wolf, bear, leopard, horse, and ass . . . ." So wrote the Greek physician Soranus (27) in the second century A.D., formulating with greater emphasis a suspicion that had existed much earlier. Thus, the role of the dog as an important vector in the transmission of rabies to man was recognized long ago, and it is no wonder that Pasteur's first efforts to control rabies were directed toward the immunization of dogs (24). Pasteur's vaccine consisted of spinal cord virus which had been modified or "fixed" by serial intracerebral passage in rabbits, and further attenuated by desiccation at room temperature over potassium hydroxide. Dogs were made resistant to rabies by a series of 10 daily subcutaneous injections of the fixed virus which had been graded from no infectivity to maximum infectivity according to tests in rabbits inoculated intracerebrally.

From Pasteur's pioneering work through the 1940's, canine rabies vaccines employed in all parts of the world were essentially modifications of Pasteur's original vaccine. All originated from infected nervous tissues of a variety of mammalian hosts; some contained live attenuated virus, and others consisted of inactivated virus. One vaccine that has had extensive use, both in this country and elsewhere, is the Semple (25) modification of Fermi's (8) phenolized vaccine.

In 1945, Johnson (13) showed that a single injection of a Semple-type brain tissue vaccine produced a high degree of resistance in dogs to heavy challenge with street rabies virus, and that 88.5 percent of the dogs were still immune 12 months after vaccination. Johnson also indicated that, as with other inactivated virus vaccines, a higher rate of protection was obtained by three weekly injections than by the single dose.

Ultra-violet light successfully inactivates nervous tissue fixed rabies virus; but irradiated vaccines, although proved immunogenic, have had little use in the field (11, 12). It cannot be denied that inactivated rabies vaccines, prepared under optimal conditions, have rendered real service in the protection of dogs against natural exposure. Yet these vaccines cannot be considered free of serious drawbacks. First, the immunity they induce is often short-lived, so that annual revaccinations are imperative. Secondly, nervous tissue vaccines sometimes induce neuroparalytic accidents (3).

In-ovo Chicken Embryo Vaccine. A radical departure from nervous tissue rabies vaccine for dogs was made when the Flury strain of rabies virus was propagated in the chicken embryo by Koprowski and Cox (20), after Johnson (14) had passed the original infected human tissue intracerebrally through 136 transfers in day-old chicks. Virus from the fortieth to fiftieth chicken embryo passages was designated LEP (low egg passage) (19) and was completely avirulent for dogs injected parenterally. The animals developed full immunity.

It is redundant to state here that provided it is of adequate potency LEP virus has been and continues to be highly successful in immunizing dogs against rabies. Suffice it to say that the early laboratory experience was followed by many countrywide and citywide tests which amply confirmed its safety and efficacy, and that its performance has continued to be good in routine veterinary practice and mass vaccination campaigns. As time has passed, progress has been made in defining with greater precision the conditions for optimal results with LEP vaccine in dogs. For example, it was shown that puppies less than 11 weeks of age do not respond as well as older animals (15). These and similar findings are the basis for the recommendations that LEP vaccine not be used before a puppy is 3 months old, and that any animals vaccinated before that age be revaccinated (32).

The initial experimental LEP vaccines were freeze-dried preparations of 20 to 40 percent infected chicken embryo suspensions, from which only gross tissue fragments were removed by passage through coarse mesh clarifiers. The dog dose of vaccine was subsequently arbitrarily set at 3.0 ml of the grossly clarified 33 percent

[1]Lederle Laboratories, American Cyanamid Co., Pearl River, New York.

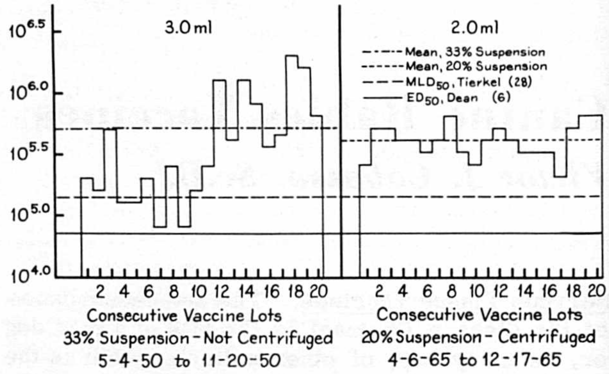
suspension, a dose amply effective when administered intramuscularly. This dog dose was ultimately adopted by the WHO Expert Committee on Rabies as representing the minimum requirements for LEP rabies vaccines, with the infectious titer of these vaccines relegated to secondary importance (31, 32). But it was a vaccine lot containing 40 percent tissue, rather than 33 percent, prepared and used as above, which Tierkel et al (28) tested in dogs for duration of immunity. They reported 100 percent protection for at least 39 months. Each 3.0 ml dog dose used in their experiment contained about 200,000 mouse LD_{50} (26).

LEP vaccines issued to the field in the early days consisted of 33 percent suspensions of infected chicken embryo, injected intramuscularly in 3.0 ml amounts. The vaccines had to pass the potency requirements formulated by the U.S. Department of Agriculture (29). In some cases, dogs developed lameness—usually transient—in the inoculated limbs. The lameness was ascribed partly to the large amount of coarse chicken embryo residue in the vaccine and partly to the relatively large volume of vaccine injected. Therefore, efforts were made to reduce tissue content and volume of dose without losing antigenicity. The suspension of infected chicken embryo was reduced to a concentration of 20 percent, and the tissue content was lessened by light centrifugation. Vaccines prepared in this way continued to pass the potency tests (29). Careful experimentation in dogs also demonstrated that a 2.0 ml dose was effective. It should be noted that a 2.0 ml dose of the 20 percent centrifuged vaccine is equivalent to 3.5 ml of an uncentrifuged preparation of the same concentration. In other words, even with the lighter tissue suspension, 40 percent of the total volume consists of tissue fragments coarse enough to be removed by light centrifugation (2000 RPM for 20 minutes).

Basing the dog dose of LEP virus on a set volume of tissue concentration was quite justifiable, pending the determination of the minimum immunizing dose. This dose has now been determined by Dean et al. (6), who titrated a commercial LEP virus lot in dogs and mice. They reported that 73,000 mouse LD_{50} were required to protect 50 percent of vaccinated dogs. It is disappointing, therefore, that this information was ignored in the 1966 WHO Expert Committee Report (32), which reiterated its recommendation for 3.0 ml of a vaccine containing 33 percent tissue and implied that only such a vaccine would result in immunity for 3 years.

In this age of quantitative virology, the only valid way to compare the potencies of two preparations of the same live virus is by measuring the live virus they contain, not by stating total tissue content. A comparison of the infective titers of

Figure 1.—*In ovo LEP rabies vaccines*
Number of Mouse LD_{50}'s in one dog dose of:



vaccines containing 33 and 20 percent tissue is shown in Figure 1. The number of mouse LD_{50} in 3.0 ml dog doses of a random set of 20 consecutive lots of 33 percent uncentrifuged LEP vaccine prepared between May and November 1950 are diagrammed side by side with corresponding values for 2.0 ml dog doses of 20 consecutive lots of 20 percent centrifuged vaccines prepared between April and December 1965. As can be seen, the titers of 33 percent vaccines varied between broader limits than those of 20 percent vaccines; between $10^{4.85}$ or 80,000 mouse LD_{50} and $10^{6.3}$ or 2,000,000 mouse LD_{50} for the former, and between $10^{5.3}$ or 200,000 and $10^{5.8}$ or 630,000 mouse LD_{50} for the latter. Mean values were, however, quite similar for the two vaccines: i.e., $10^{5.7}$ or 500,000 mouse LD_{50} for 33 percent tissue vaccines, and $10^{5.6}$ or 400,000 mouse LD_{50} for the 20 percent tissue vaccines. The mean value of the 33 percent preparations was 7 times the ED_{50} determined by Dean et al., (6) and the mean value of the 20 percent preparations was 6 times greater.

The speculation has been advanced that the higher concentration of tissue in the 33 percent suspension vaccines, acting as adjuvant, would result in a higher degree of immunity. The higher immunogenic ability of an essentially tissue-free tissue culture LEP vaccine demonstrated by Dean et al. (6) and by us (5) militates against the validity of such a speculation. The statement that only "a dose of 3 ml of a 33 percent vaccine . . . should be the minimum dose if an effective immunity of three years is desired" (31) would be difficult to support in view of the comparison shown in Figure 1, which reveals that the mean infective titers of 33 and 20 percent tissue vaccines are essentially the same. Another point worth emphasizing is that only one vaccine lot was used in the 1947 experiment on duration of immunity, and that it contained 40 percent tissue (26). Furthermore, although the titers of 33 percent tissue vaccines issued for field use have varied appreciably on either side of the values for the vaccine lot used in 1947, their ability to protect dogs for 3 years remains unquestioned. Finally, infective titers of consecutive lots of 20 percent tissue vaccines compare very favorably with those of the 1947 vaccine.

Tissue Culture Vaccines. The increasing use of tissue culture for virus study led to its application to investigations with rabies virus (2, 9, 10, 16, 17, 21, 30), and thus inevitably to the preparation of inactivated or live rabies vaccines in a variety of tissue culture systems (1, 5-7, 18, 22, 23). This presentation will be concerned only with LEP vaccine prepared in chicken embryo tissue cultures. Our laboratory has previously reported that the LEP strain of rabies virus had been propagated serially in chicken embryo tissue cultures, yielding mouse LD_{50} titers ranging from $10^{4.0}$ to $10^{6.0}$ per 1.0 ml of pooled fluids and cells (4, 5). The considerable accumulation of rabies antigen in the cytoplasm of infected cells is made evident by immunofluorescence (Figures 2 and 3).

Table 1 summarizes results obtained with consecutive lots of freeze-dried LEP tissue culture vaccines in guinea pigs and in dogs. The mouse LD_{50} content of 2.0 ml dog doses varied between 20,000 and 400,000. Four of the seven lots, at a 1:80 dilution of a dog dose, failed to pass the potency test set forth by the U. S. Department of Agriculture (29). However, close to 40 percent of the guinea pigs given this inoculum were protected against challenge, and some of the vaccines that failed the test had infective titers equivalent to those of vaccines that passed. Furthermore, vaccine that passed the test at 1/80 of a dog dose in our laboratory did not do so at 1/48 of a dog dose in another laboratory (6). Vaccines 4 and 6, with infective titers differing by a factor of 6, both protected only about 35 percent of guinea pigs given 1/80 of a dog dose. When retested with 1/8 of a dog dose, each protected 100 percent of the animals.

Despite the failure of some of these vaccines to pass the prescribed potency test, all those used protected dogs against challenge with street rabies virus 2 to 3 months after a 2.0 ml dose. Vaccine 7, with 20,000 mouse LD_{50}/2.0 ml, was as effective as vaccine 2 with 400,000. Vaccine 3 was equally effective whether dogs were given 320,000, 32,000, or 5,000 mouse LD_{50} in a single 2.0 ml intramuscular injection.

Fifty-nine of 60 vaccinated dogs (98.3 percent) resisted challenge, and 51 (85.0 percent) had demonstrable serum neutralizing rabies antibody (titer of 1:2 or higher) shortly before or at the time of challenge. The one dog that died after challenge had no detectable antibody. In contrast to the vaccinated dogs, 28 of 32 (87.5 percent) unvaccinated control dogs succumbed to challenge, and none of the 32 had detectable rabies antibody.

Figure 2.—*Accumulation of rabies antigen in cytoplasm of chicken-embryo tissue culture cells infected with LEP Flury strain virus. Immunofluorescent staining X1600.*

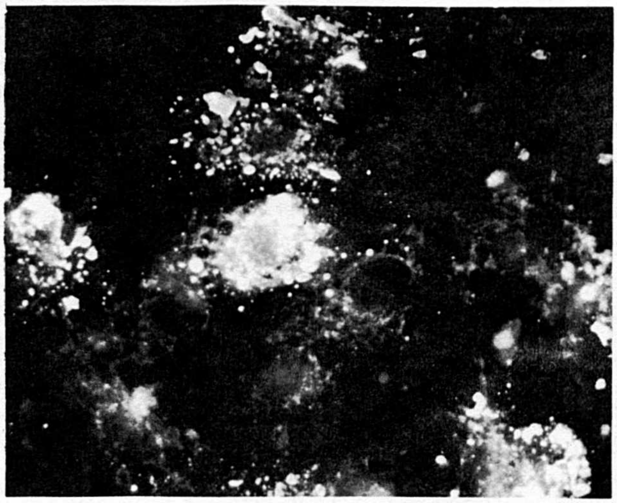


Figure 3.—*Accumulation of rabies antigen in cytoplasm of clump of chicken-embryo tissue culture cells infected with LEP Flury strain virus. Immunofluorescent staining X640.*

Table 2 presents the results of challenge with street rabies virus 1 year after dogs had been inoculated with vaccine from one of three lots. Thirty of 32 (94 percent) vaccinated dogs survived, while 29 of 30 control dogs died following the same challenge. One month after vaccination, all 25 of the dogs receiving vaccines 2 or 3 had measurable rabies antibody. One year after vaccination, 24 of the 32 animals were serologically positive, although antibody levels were considerably lower than those measured at one month.

Neither of the vaccinated dogs that died had detectable antibody at the time of challenge. The one given vaccine 2 died unexpectedly 9 days after

Table 1.—*LEP tissue culture rabies vaccine potency testing in guinea pigs of consecutive vaccine lots, and response of dogs 2-3 months after vaccination*

[No dogs had antibody detectable at 1:2 dilution when vaccinated]

Vaccine lot number	Mouse LD_{50} per 2.0 ml dog dose	Guineapig test with fraction of dog dose			Results in dogs		Remarks
		1/80th	1/48th	1/8th	Surviving challenges	Serological response	
1	250,000	[1]10/11	[2]7/14	Not tested	[1]13/13	[3]9/13	
2	400,000	9/10	Not tested	Not tested	3/3	3/3	
3	320,000	9/10	Not tested	Not tested	10/10	10/10	
3	32,000	Not tested	Not tested	Not tested	7/7	6/7	
3	5,000	Not tested	Not tested	Not tested	9/9	8/9	
4	50,000	4/9	Not tested	9/9	Not tested	Not tested	
5	160,000	5/10	Not tested	Not tested	Not tested	Not tested	
6	320,000	[4]8/22	Not tested	9/9	8/9	8/9	Dog that died – Neg. serology
7	20,000	3/12	Not tested	Not tested	9/9	7/9	
Total					59/60	51/60	
Percent					(98.3)	(85.0)	
Unvaccinated Controls					4/32	0/32	
Percent					(12.5)	(0)	

[1]Number surviving/total.
[2]Test carried out by different laboratory.
[3]Number positive/number tested: Serum neutralizing antibody titer of 1:2 or higher.
[4]Summation of 2 tests.

Table 2.—*LEP tissue culture rabies vaccine in dogs – Antibody status and resistance to challenge 1 year after vaccination*

[No dogs had antibody detectable at 1:2 dilution when vaccinated]

Vaccine lot number	Mouse LD_{50} per 2.0 ml dog dose	Number surviving challenge	Number of dogs with antibody at		Remarks
			1 month	1 year	
1	250,000	[1]6/7	Not tested	[2]2/7	Dog that died – Neg. serology
2	400,000	12/13	13/13	10/13	Dog that died – Neg. serology
3	320,000	12/12	12/12	12/12	
Total		30/32	25/25	24/32	
Percent		(94.0)	(100)	(75.0)	
Unvaccinated controls		1/30	Not tested	0/30	
Percent		(3.3)		(0)	

[1]Number surviving/total.
[2]Number positive/number tested: serum-neutralizing antibody titer of 1:2 or higher.

challenge, with no sign of illness. This dog appeared normal at necropsy; neither staining nor immunofluorescence revealed Negri bodies in its Ammon's horn, and no virus was recovered from its brain by mouse inoculation. It had showed the lowest antibody titer in the No. 2 group a month after vaccination. The control dogs died between days 10 and 25 after challenge, following 1 to 3 days of illness evidenced by tremor, salivation, weakness, and paralysis. Other vaccinated and control dogs are being held for challenge 3 years after vaccination.

The perfect correlation between presence of rabies antibody in vaccinated dogs and their

Table 3.—*LEP tissue culture rabies vaccine in dogs —Correlation between presence of rabies antibody and resistance to challenge*

[No dogs had antibody detectable at 1:2 dilution when vaccinated]

Interval between vaccination and challenge	Number of dogs				
	Total	With antibody[1]	Without antibody[2]	Surviving challenge	
				With antibody[1]	Without antibody[2]
2-3 months	60	51	9	51/51	8/9
1 year	32	24	8	24/24	6/8
Total	92 (100%)	75 (81.5%)	17 (18.5%)	75/75	14/17
Percent of dogs surviving challenge				100	82.3
Control dogs	62 (100%)	0	62 (100%)	Not tested	5/62 (8%)

[1]Serum neutralizing antibody detected at a dilution of 1:2 or higher.

[2]No antibody detected at a serum dilution of 1:2.

resistance to challenge is evidenced by the data in Table 3 — not one of 75 vaccinated dogs with antibody at the time of challenge died. Absence of antibody in vaccinated dogs, however, does not necessarily denote susceptibility to challenge, as 82.3 percent of dogs in this category also survived.

In another experiment, graded doses of vaccine 3 were administered to dogs for the purpose of establishing the number of mouse LD_{50} of virus that would protect 50 percent of the animals. This was found to be the equivalent of 1,220 mouse LD_{50}, a value corresponding well to that of 350 mouse LD_{50} obtained by Dean et al. (6) for the same type of vaccine, and differing appreciably from that of 73,000 mouse LD_{50} calculated by the same authors for conventional in ovo LEP vaccine.

Finally, 2,443 dogs of many different breeds, ranging in age from 3 months to 16 years, were vaccinated in the field by a number of veterinarians. The dogs received single 2.0 ml doses of chicken embryo tissue culture vaccine from the seven lots described above. Of the nine unfavorable reactions reported, all were transitory and none were serious. Six were local, characterized by pain at the injection site for a few hours to a few days, and occurred mainly in Chihuahuas. The other three reactions were anaphylactoid and of short duration.

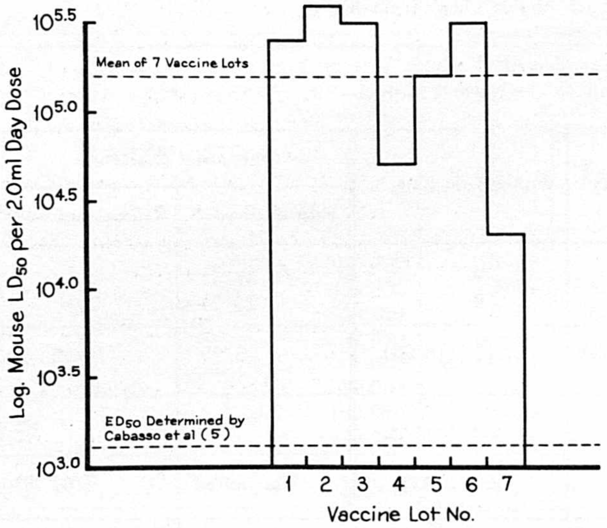
Immune response under field conditions was evaluated by testing pre- and post-vaccination sera from 97 dogs of seven breeds. Each received vaccine containing 50,000 mouse LD_{50} per 2.0 ml. Eight of the dogs had detectable rabies neutralizing antibody before being given the tissue culture vaccine, and five of these were found to have been vaccinated against rabies 1 to 2 years earlier. All 89 dogs without pre-vaccination antibody had developed antibody, which did not vary appreciably among breeds, 1 month after inoculation.

The marked discrepancy between the results of the prescribed potency tests in guinea pigs and the performance of the chicken embryo tissue culture vaccine in dogs signifies the need for a different approach in setting the potency requirements for production vaccines. Such an approach could take into account the two parameters developed in our studies: the minimum dog-immunizing dose (ED_{50}) of the vaccine, and the high degree of correlation between presence of antibody and resistance to challenge. The validity of the first parameter is illustrated in Figure 4, which shows that the seven vaccine lots exceeded the established ED_{50} by factors ranging from 16 to 320, the mean titer of $10_{5.2}$ or 160,000 for a 2.0 ml dog dose being about 125 times the ED_{50}. This compares with 6 to 7 times for conventional in ovo vaccine. The validity of the second parameter rests on the fact that not a single dog with measurable antibody at the time of challenge succumbed to rabies.

Summary and Conclusions. Canine rabies vaccines can be prepared from infected mammalian nerve tissue, from chicken embryos in ovo, and from cultures of various tissues, including the chicken embryo. Inactivated nervous tissue vaccines have proved their effectiveness and have rendered real service. Their drawbacks are the necessity for repeated vaccination and the possibility of neuroparalytic accidents.

Extensive use of chicken embryo LEP vaccine prepared in ovo has amply proved its safety and efficacy. Immunity in dogs following a single

Figure 4.–*Tissue culture LEP rabies vaccine No. of mouse LD_{50} in one 2ml dog dose*



vaccination has been demonstrated to last more than 3 years. Increased knowledge demands that the earlier arbitrary values for vaccine suspensions and volume of dog dose be re-examined, so that the dose requirement can be based on infective titer rather than on concentration of chicken embryo tissue.

Finally, the immunizing effectiveness of LEP vaccine prepared in chicken embryo tissue cultures has been demonstrated in several experiments in which dogs were directly challenged with street rabies virus. Dogs given a single 2.0 ml dose of the tissue culture vaccine were still immune a year later. Additional dogs are being held for challenge 3 years after vaccination. The dose that protected 50 percent of the inoculated dogs was found to be the equivalent of 1,220 mouse LD_{50}, and there was a 100 percent correlation between presence of antibody and resistance to challenge. Despite the demonstrated effectiveness of several lots of LEP tissue culture vaccines in dogs, some did not pass the prescribed potency test in guinea pigs at the level of 1/80 of a dog dose. Potency requirements based on vaccine infectivity titer and serologic conversion of vaccinated dogs are recommended.

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Hamster Cell Culture Rabies Vaccines

George L. Ott, Ph.D.[1]

Using Kissling's basic cultural methods with the hamster kidney cell culture system, two cell culture origin vaccines for use in dogs, cats, and other animals have been developed and are being used in the veterinary field. One, using strain CVS mouse-fixed rabies virus, is phenol-inactivated. The other, using the already attenuated Flury strain chick embryo origin virus, is a live modified virus vaccine. Both vaccines are tested before release under Agricultural Research Service Standard V-11 potency testing requirement, in which test animals are injected once, and subjected to intramuscular challenge with virulent CVS rabies virus 21 days postvaccination.

To be released for distribution under official ARS standards, 80 percent of the unvaccinated controls must succumb to rabies challenge, and at least 70 percent of the vaccinates must survive. Supportive data in dogs, foxes, and cats, together with pre- and post-vaccination serological studies in these species has been presented. Hamster kidney cell origin rabies vaccines, shown to be effective either as inactivated or as attenuated vaccines, also possess the advantage of being propagated in non-nervous tissue and can be prepared as cell-free products, thus reducing postvaccination tissue reactions to a minimum.

[1]Fromm Laboratories, Inc., Grafton, Wisconsin.

Vaccination of Domestic Animals with a Rabies Vaccine Produced in Tissue Culture from the ERA Strain

M. K. Abelseth, D.V.M.[1]

A rabies virus isolate originally obtained from a rabid dog was adapted to hamster kidney by Dr. P. Fenje after successive passages in adult mice. The virus obtained from Dr. Fenje was serially passed 10 times through chick embryo before adapting to pig kidney tissue culture. At the sixth passage the strain was named "ERA" for identification purposes. At that passage level a titer of $10^{-3.3}$ mouse LD_{50} was reached, and cattle vaccinated with it survived a challenge of street rabies virus. One hundred passages have resulted in a titer of $10^{-4.5}$ to 10^{-6} LD_{50} per mouse inoculation.

The ERA virus strain is pathogenic for mice, guinea pigs, and hamsters by the intracerebral route, but it has a very low degree of virulence by the intramuscular route. It is apathogenic for domestic animals by the intramuscular route. The ERA strain meets the vaccination and challenge tests required for the Flury strains of rabies vaccine.

Vaccination of dogs, sheep, and cattle with the vaccine in dilutions up to 1:1000 followed by challenge indicates a high degree of antigenic response. Vaccination of cats, dogs, sheep, goats, cattle, and horses with a single dose of freeze-dried vaccine protected these animals against challenge which usually resulted in 95 to 100 percent mortality of the non-vaccinated controls.

Duration of immunity studies as measured by challenge have shown protection for at least 2 years in dogs and 3 years in cattle. The challenge virus utilized for measuring immunity was a preparation of fox salivary glands from naturally infected field cases.

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Discussion--Canine Rabies Vaccines

G. V. Peacock, D.V.M.[1]

Papers on canine rabies vaccine which have been presented here emphasize the rapid trend toward propagation of rabies virus in cell cultures for preparation of both attenuated and inactivated vaccines. The change to this method of virus production is stimulated by the occasional undesirable reactions that occur in dogs following use of nervous tissue origin or chicken-embryo origin rabies vaccines, and by rapid advances in virology.

Dr. Cabasso, Dr. Abelseth, and Dr. Ott have summarized and supplemented published data which conclusively establishes the efficacy for dogs of three different attenuated rabies vaccines prepared from cell culture virus fluids. These papers justify increased use of cell culture rabies vaccines in spite of the fact that efficacy of chicken-embryo, low egg passage Flury virus rabies vaccines generally has been greatly improved during the last 5 years.

The Veterinary Biologics Division of the Agricultural Research Service is responsible for enforcement of the Virus-Serum-Toxin Act of 1913. This Act prohibits interstate sale or shipment of biological products for the treatment of domestic animals and poultry except as authorized under a license or permit issued by the Secretary of Agriculture. Because of the large number of different veterinary biological products and for practical reasons, our Division has not had the opportunity to evaluate rabies vaccines properly in dogs. Reports by Dr. D. D. Dean, of the New York State Department of Health, prompted the Division to conduct extensive evaluations of LEP chicken-embryo origin modified live virus vaccines in 1961.

Screening studies (8) consisting of virus titrations in mice and guinea pig potency tests confirmed Dr. Dean's findings. Corrective action by the Division included an overall reduction in permitted dating periods and restraints on further marketing by some licensees until satisfactory improvement had been demonstrated. Cooperative efforts by the biologics industry, which included extensive stability testing programs, resulted in marked improvement in chick-embryo origin low egg passage modified live Flury virus rabies vaccines. Continuing evaluations by the Division at the National Animal Disease Laboratory have shown that the potency of this product is being maintained at a high level and that stability failures now very rarely occur.

As a result of confirmed reports of virulence for cats, label recommendations for this type of vaccine are now limited to dogs. The Division is developing higher standard requirements for purity and safety for attenuated chicken-embryo origin rabies vaccines. Kissling's (6) first report of growth of rabies virus in non-nervous tissue culture was followed by extensive research efforts by Fenje (5), Ott (9), Dean (4), Cabasso (3), Abelseth (1, 2), Wiktor (10), and others. Although the Veterinary Biologics Division has not evaluated these experimental cell culture propagated vaccines in dogs, we have had the somewhat unique opportunity of reviewing unpublished data furnished by each applicant for license or permit. In contrast to limited studies of chicken-embryo origin vaccines in dogs, overall evaluations of experimental cell culture propagated products involve serology and challenge tests in hundreds of dogs and several individual domestic animals of other species.

Drs. Cabasso, Abelseth, and Ott have indicated that cell culture propagated modified live virus rabies vaccine appears to be very efficacious in dogs. However, the efficacy of different cell culture rabies vaccines varies quite markedly when evaluated in guinea pigs. There are data indicating that vaccine which is effective in guinea pigs given 1/80 dog dose will consistently protect dogs against a virulent challenge. However, as Dr. Cabasso has shown, for some tissue culture vaccines there is little correlation between evaluations by these two methods. Further studies on newly developed rabies vaccines may reveal differences in mouse virulence as well as antigenicity for guinea pigs, which have resulted from virus modifications in various laboratories. At present, it appears that the quantity of living vaccine virus is the greatest single factor relative to guinea pig protection. It is interesting to note that a single 1.0 ml dose of properly prepared inactivated virus hamster cell culture rabies vaccine will routinely protect guinea pigs against either "street" or "fixed" rabies challenge virus.

Each license applicant has been required to conduct protective titrations in dogs for information relative to efficacy in dogs in terms of

[1]Veterinary Biologics, U.S. Department of Agriculture, Washington, D.C.

mouse infectivity and to demonstrate the minimum acceptable vaccine virus titer represents several effective dog doses. Results of these minimum protective dose studies have varied considerably in different experiments using the same vaccine as well as in separate tests on various types of cell culture propagated products. Serological results have also been variable. Considerable uncertainty has developed relative to these points. Apparently there is a broad range in the ability of individual dogs to respond to rabies vaccine. However, considering the inherent experimental errors in both the infectivity and protective titrations, overall results of minimum protective dose studies for several vaccines fall within an expected range.

Our conclusions relative to data presented by biologics manufacturers include:

1. Modified live virus tissue culture origin rabies vaccines, have a common ability to protect dogs in relatively high dilutions. The major practical difference between various separate tissue culture origin vaccines is the degree of virulence for species of animals more susceptible than dogs.
2. The average virus titer, measured in mouse LD_{50}, in most tissue culture origin vaccines is somewhat lower than virus levels common for chicken-embryo origin products.
3. Challenge tests in dogs are possible and most significant, although such evaluations on a routine basis appear needlessly inhumane and dangerous to personnel.
4. Satisfactory guinea pig protection by cell culture vaccines using dosage levels required for chicken-embryo products is a positive indication of efficacy for dogs. However, like serological tests, unsatisfactory results in guinea pigs are less conclusive.
5. Serological tests are quite reliable for evaluating efficacy of rabies vaccines in dogs. However, the neutralizing antibody titer which consistently assures protection against challenge has not been conclusively established.

The Division has the problem of evaluating rabies vaccines prepared under license or for which applications for license or permit are received. Uniform requirements and test procedures are desirable for tissue culture origin rabies vaccines. Reports of contaminating viruses in some laboratory strains of rabies virus must be considered (11). The Veterinary Biologics Division is evaluating tests to detect lymphocytic choriomeningitis virus and will screen vaccines for this possible contaminating agent. Guinea pig potency tests using undiluted vaccine are being considered to determine if increased dosage levels will provide a practical and valid test for antigenicity.

Tentative requirements for each serial of attenuated cell culture propagated rabies vaccine include cultural and animal tests to detect pathogenic contaminating agents, virus titrations in mice with a minimum virus level of $10^{4.5}$ LD_{50} per dog dose which must be maintained throughout the permitted dating period, and challenge tests for antigenicity in guinea pigs or dogs. Eventually a standard serological test in dogs may be adopted.

There is valid evidence that tissue culture origin rabies vaccines are equal or superior to chicken-embryo origin products. Although stability and duration of immunity must be studied further, the immediate problem is adequate requirements to be met by each serial.

Combined efforts of regulatory, research, public health, and commercial workers should assure the availability of more effective rabies vaccines which do not cause the undesirable reactions sometimes associated with use of nervous tissue origin and chicken-embryo origin vaccines.

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Urban Rabies Control

Joseph D. Salisbury, D.V.M.[1]

The principles of complete rabies control have been adequately put forth. Tierkel's (1) statement of these in his paper to the U.S. Livestock Sanitary Association in Kansas City in 1951 are just as valid today as when expressed. He listed adequate diagnostic procedures, accurate reporting systems, elimination of stray animals, registration of dogs, canine rabies vaccination, and wildlife control programs. To these may be added what these imply and require, public education.

Many cities have adopted these points in their programs, usually under the guidance of competent public health veterinarians. Their success has been attested to by the virtual elimination of canine rabies from the geographical boundaries of such cities as Memphis, Denver, St. Louis, Houston, San Antonio, Los Angeles, Chicago, and Indianapolis, to mention but a few.

What is painfully obvious is that every center of urban population has its dog problem, i.e., increased population, straying animals, the threat of a canine disease of epidemic proportion be it rabies or some other disease. The methods of handling these problems are widely variable. In many areas they are handled by the police department, in others by contract with the humane societies, and in still many others by the health department or an independent division of municipal government especially created for such purpose. In most cases the objectives remain the same—the eventual elimination of rabies from the canine population howsoever the issue becomes beclouded by selfish interests or motivations. Dog control and attendant rabies control cannot be swept under the rug or ignored, regardless of how much urban administrative authorities may wish it so. When cases are at a low ebb or non-existent, officials and the public tend to feel secure and become lackadaisical. This frequently finds expression in lowered appropriations to operate shelter facilities, lowered number of canine vaccinations, less registration or licensure, and, too often, the reduction in control activities. This is precisely the time a good public health education program is most needed.

Corollaries can be drawn with several of the human disease pictures where the "immune level" of the population has tended to drop off followed by the occurrence of cases of a disease not seen in the community for 15 or 20 years. Witness the incidence of diphtheria in several areas where this chain of events has occurred. So it may be with rabies, where communities are always subject to the introduction of cases from outside. That this importation of a rabid animal does occur was painfully brought out recently in my community, where the first rabid dog in more than 5 years proved to be an import just 3 weeks prior to its death from the disease. This occurred coincident with the time when our community was completing an energetic vaccination program in association with the local veterinary society. Newspaper and TV reporters had strongly supported the program. Intensified stray pick-up cruises had been instituted. Investigators covered the immediate community notifying people to have their unvaccinated pets vaccinated by the local veterinarians. We hope our efforts have been successful, but we are keeping a wary eye on developments. So far there have been no additional cases in the 5 weeks which have elapsed.

Other factors in the epidemiology of canine rabies are ruefully at work in urban areas. The trend toward urbanization of the human population with its forecasted megalopolis brings with it a larger dog population—at least this has been so until just recently, when the dog population seemed to stabilize, according to the feed manufacturers, but I think it merely a hesitation—and increases the chances for contact between dogs. As these areas spread, then the pets on the periphery have greater probability of contact with wildlife species which may be infected with the disease, hence the possible introduction of the infectious agent. Without zealous control efforts, this portends the possible shift of rabies from enzootic to epizootic proportions. However, the introduction of the causative agent may come from those creatures of normally nocturnal habits, the bats. Thus any area of a city may unsuspectingly have the seeds of an epizootic sown at any time. Again this points up the demands for good health education to illuminate for the public the necessity of keeping their pets vaccinated. This activity is calculated to offset the greatest liability in rabies control programs of "ignorance, misconceptions, and

[1]San Antonio Health Department, San Antonio, Texas.

general lethargy on the part of a substantial number of our population'' as Tierkel (2) so aptly stated it.

Many cities have successfully carried out mass vaccination programs in the face of epizootic outbreaks of rabies. These are aimed at vaccinating the largest number of owned dogs in the shortest period of time. Rabies control officials have received public cooperation in restraining owned dogs at such a time, so that unowned, unvaccinated stray dogs can be picked up off the public streets. Even carefully planned wildlife reduction programs have been carried out without incurring extensive public criticism at a time like this. In the throes of an epizootic, these activities take on the air of the dramatic event. Listen to the emphasis given to some news announcements by radio reporters of events surrounding the biting episode of a suspected rabid animal. At such times you get public reaction and action. Under these circumstances, urban rabies control is far less difficult.

But let the other face of Janus be seen. When cause for alarm does not exist, dog control to continue rabies control becomes a rockhard difficult job. At times like these, the public can see no need for the villian of the comic strips, the proverbial ''dog-catcher,'' to continue his preying ways. The animal warden must at once be a philosopher, psychologist, hard-nosed cop, perhaps track star, and sympathetic father-type all rolled into one.

Therefore, to accomplish the objectives of rabies control, governing bodies of cities or urban areas must pass ordinances enabling those upon whom this responsibility is placed to carry out their duties. Before ordinances are passed or amended the objectives of such ordinances must be established. These may be but are not limited to:

(1) Control of rabies outbreaks.
(2) Prevention of nuisances (barking dogs, roaming).
(3) Establishment of a revenue measure.
(4) Combination of any or all of the above.

A good animal control ordinance will provide safeguards for people and for animals. It will place the responsibility on and give authority to a designated agency of government for carrying out the provisions of its sections. Usually a combination of objectives is desired.

Consideration must be given to promulgating sections of the ordinance pertaining to each and every phase of the operation. Words or terms used, such as ''valid vaccination certificate'' and ''recognized vaccine,'' should be carefully defined. A common basis of understanding must be established so that lawyer, layman, and medical person all interpret the phraseology alike. In addition to a section on definitions, an ordinance should include sections on the following:

(1) Provision of an impounding facility, whether operated by a city department or a contract agency. Experience has indicated considerable success has been obtained under health departments whose public health veterinarians exercise jurisdiction over the operation, or are utilized as consultants on management. This is not the only way, nor is it infallible, but it has met with wide success.

(2) Requiring antirabies vaccination by stipulating earliest age for required vaccination, naming species if desired, and as a prerequisite to registration or licensure. The recognition of type of vaccine may be stated and an established period of immunity may be recognized.

(3) Requiring a license or registration if desired, the period for which issued, and establishing a fee. If vaccination is to be a prerequisite for licensure of registration, consideration should be given to the administrative feasibility of the requirements. Tierkel states that rabies problems will not be solved by depending on the sporadic, voluntary vaccination of dogs in veterinary hospitals, staggered throughout the year. Provision for a penalty clause for failure to comply should pertain to all sections requiring the public's compliance.

(4) Impounding of dogs running at large. This usually is effected at the governmentally provided shelter, and, where leash laws exist, should apply to both licensed and unlicensed dogs; otherwise just the latter.

(5) Impounding of biting animal. This facet is imperative to rabies control.

(6) Establishing periods of impoundment, such as for strays 3 days and for biting animals 10 days, or 10 days following the bite episode.

(7) Providing for fees for reclaiming impounded animals and boarding fee while the animal is impounded.

(8) Requiring that no animal be released without evidence of valid vaccination and registration or license if required, and certification by a veterinarian that the animal is free of rabies symptoms.

(9) Requiring the reporting of all animal bites to the proper agency and placing responsibility for this reporting. There also should be stated any incumbency upon the agency to follow up all reported bites. This must include obtaining all of the necessary epidemiological data and information necessary to effect observation of the offending animal.

(10) Requiring that animals bitten by known rabid animals be destroyed, or confined for 6 months at the owner's expense, or, if currently vaccinated, revaccinated and confined for 30 days. These are in accord with the WHO Expert Committee on rabies recommendations.

(11) Making provision for the disposition of impounded animals. These include return to owner, casual sale to public to be a pet, sale to reputable research organizations operating facilities approved by a designated authority and subject to un-announced inspection by the responsible agency, and euthanasia for unclaimed impounded animals, with necessary safeguards, and unwanted animals presented for humane disposition.

Certain other provisions should be considered. These are in the area of restraining individuals who consider an animal warden, in the proper exercise of his duty, to be fair game for their reprisals, such as releasing an animal from a pick-up vehicle, turning loose all animals on a truck, forcing the truck off of the road or to the curb, and many other unreasoned actions.

The promulgation of ordinances merely creates the legal authority whereby certain functions can be carried on. If urban administrative bodies do not provide the budget for carrying out the intent of the rabies control or animal control ordinance it will be of no avail. Careful considerations must be given to budgetary requests. Sufficient personnel must be available to operate the facility and equipment, and sufficient equipment including rolling stock must be available to cover the jurisdictional area. Fees collected for licensing, impoundment, and boarding should not be expected to support this public health measure. In fact the largest proportion of funds to successfully operate the facility and properly discharge the responsibilities of an urban rabies control operation must come from appropriated funds.

Fiscal and animal accountability are an absolute must so far as proper shelter operation is concerned. Many administrative records and forms, in our operation, were devised by representatives of the Cities' Internal Audit Section. This section conducts audits of both animal and cash receipts as Shashek (3) reported occurs in St. Louis. It is the only way we can be assured of proper operations from an accountability standpoint. Fiscal and animal accountability are an absolute must so far as proper shelter operation is concerned. Many administrative records and forms, in our operation, were devised by representatives of the Cities Internal Audit Section. This section conducts audits of both animal and cash receipts as Shashek (3) reported occurs in St. Louis. It is the only way we can be assured of proper operations from an accountability standpoint.

Our shelter also is visited daily by a veterinarian from the local veterinary society who vaccinates all animals due for release, in addition to observing the health of the animals in the shelter and making suggestions to help with the efficiency of the operation. The principles of sanitation are not overlooked.

An adequate education and training program for all rabies control personnel is a must. It is too much to assume that people who have not had 6 months or more of experience in the operation can function without supervision. Refresher activity for rabies control investigators and the facility supervisor are not too much to ask for. At the salaries normally paid to animal shelter personnel, you can expect to employ only the caliber people who need frequent counseling and almost constant supervision. Administrative safeguards and counter checks should be instituted to keep track of the operations. This rather sensitive area of city function when operated efficiently and smoothly can reflect much credit upon city administrations.

I am especially pleased with the budgetary considerations shown to Rabies Control Section of my Division of Veterinary Services of the San Antonio Metropolitan Health District by responsible governmental administrative officers.

I should like to conclude by stating that principles of urban rabies control are the same today as they were 20 years ago—certain adjuvants have been improved, and only tenacious adherence to those principles will result in maintaining the progress realized to date and the eventual goal of eradication of the disease from man's frequent associates, his pets.

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Discussion--Urban Rabies Control

Robert F. Willson, D.V.M.[1]

Discussion of the efficacy of vaccines, ecology, rabies reservoirs, pre-exposure vaccine, and sylvatic rabies is worthwhile and informative. I think that we are all agreed that immunization and control of the stray animal are primary steps in the regulation of the disease. One cannot help but observe that some mention should be made about that important, but little known segment of the public health team, the dog wardens or dog-catchers. This group is a much maligned and "looked down-upon" group. They occupy a place on the social scale a little above the broken-down politican who "couldn't be elected dogcatcher."

In Detroit we have included the poundmaster and his assistant in all of our staff meetings. All of the employees of the dog pound attend our in-service training programs. We are constantly boosting their efforts to the newspapers. Despite all these efforts, our men are daily kicked, beaten, reviled, and in one instance run-over by the automobile of an irate dog owner.

I would hope that those of you who have to do with dog wardens and dog pounds would try to change the image of this group of loyal men. This can be done by creating a good press, providing modern equipment, and instituting training programs. Possibly CDC would investigate and formulate a training program for dog wardens in order to elevate this individual to his proper place in the control program and public acceptance.

It is my sincere hope that one recommendation which could come out of this symposium would be a recommendation for a kinder attitude of the public toward the dog catcher. He is not a dog-napper, a sadist, or a vivisectionist. He is an honest, loyal, person trying to do an almost impossible job. I say "BE KIND TO THE DOG-CATCHER."

[1]Detroit Health Department, Detroit, Michigan.

Discussion--Urban Rabies Control

Jeroham Asedo, D.V.M.[1]

This year the New York City Health Department is celebrating the Centennial Anniversary of its organization. Health Department records from the year 1907 to date indicate a constant struggle to eradicate rabies. What preceded 1907 is not fully recorded, but mention is made of the fact that Pasteur vaccine was used from 1898 to 1908 and then, with some modification in its preparation, until 1913.

Table 1.–*Dog bites and rabies cases New York City–1908-25*

Year	Number of dog bites	Number of rabies cases	Rabies in humans
1908	4,622	104	0
1909	5,168	57	0
1910	3,792	75	0
1911	4,509	212	0
1912	4,192	239	0
1913	4,306	268	0
1914	4,640	332	8
1915	3,640	115	1
1916	3,247	24	1
1917	2,873	31	3
1918	2,771	18	0
1919	2,778	41	5
1920	3,049	44	1
1921	3,445	85	3
1922	4,538	50	1
1923	4,099	27	3
1924	5,702	30	0
1925	7,030	76	2

Source: Bureau of Preventable Diseases, Div. of Epidemiology and Diagnosis.

Table 1 shows the number of animal bites, rabid animals, and cases of human rabies from 1908 through 1925. It is surprising to find so many rabid animals yet so few human rabies cases. It was not until 1914 that 8 human cases were reported, while there were 332 cases of rabies in animals. These 8 human cases were the first mentioned and they were the largest number in any one year in the 100-year history of the Health Department. In the period 1908-1925 there were 28 human cases, 1,820 in animals, and 75,201 bite cases.

The problems of rabies control in this city today are no different from the problems any other city in the U.S.A., but the effectiveness of any plan must take into consideration the specific prevailing conditions in a city the size of New York, which is densely populated by both men and animals. There are 8 million people and about a half million dogs, in addition to cats and other animals.

The city is composed of five boroughs. Two of them, Manhattan and Richmond, are islands, and the others are partly surrounded by the bay and the ocean and have sea- and air-ports used by men and animals from all over the world. Manhattan, some parts of Brooklyn, and the Bronx are very crowded. There is a large park in the center of each of these boroughs and a number of smaller ones in other locations. In addition, there are zoological gardens, children's playgounds, and riding academies, but no farmland or wooded areas. People love animals, and everywhere there are pet dog and cat owners. In some parts of the city, people are deliberately adopting large and unfriendly dogs, not only as pets, but for the protection of life and property. In some tenements, one may find one or more such dogs in each apartment. Having a dog in such areas becomes an absolute necessity. Many tenants living on upper floors find it easier to let their dogs out on the street unattended. Dogs flock together in groups, get into fights, and often attack passersby, especially children playing. At times the streets are crowded with people and animals thus making a fertile ground in which a rabid dog could spread disease.

No plan for the control of rabies in the city can be executed effectively without the cooperation of a number of agencies involved directly or indirectly with the health of animals or man. It is within the the duties of the Health Department through the Veterinary Division of the Bureau of

[1]Division of Veterinary Medicine, Bureau of Preventive Diseases, Department of Health, New York, New York.

Preventive Diseases to direct the main activities and enlist the help of the following:

a) the police department
b) the Society for the Prevention of Cruelty to Animals (SPCA)
c) the sanitary division of the health department
d) the veterinary association and veterinary hospitals
e) health department clinics
f) educational institutions
g) the press, public relations agencies, radio, television, etc.
h) the public in general and dog owners in particular

Rabies control in urban areas as densely populated as New York City has its limitations, its difficulties, and its advantages.

1. Rules and regulations pertaining to the care of animals are enforced by the Health Department and Police Department. The problem of strays is endless, but with the cooperation of the police, the Sanitation Department, the Sanitary Division of the Health Department, and the SPCA, conditions are kept under control. The Health Department forbids dog owners to allow animals at large in any public place, street, or park. Dogs must be restrained by a leash not more than 6 feet long.
2. Dogs must be licensed (by the SPCA).
3. All animals involved in bite incidents are reported to the Health Department and must be examined by a veterinarian.
4. Vicious dogs are destroyed by the Health Department.
5. Dogs that bite three times within a period of 2 years are destroyed by the Health Department.
6. No dog should be permitted to perform nuisances in the halls of a public dwelling.
7. No wild animals are permitted to be kept as pets by the public.

Since rabies is a reportable disease, policemen, veterinarians, physicians, or any other persons having knowledge of a rabid animal or one suspected of having rabies must report it to the Health Department. Any physician treating a person bitten by an animal must report to the Health Department immediately by telephone and follow the call up with a written report. The Health Department notifies the Police Department to have the owner of the animal served with a notice to take the animal to the Health Department shelter or to a private veterinarian for examination. The veterinarian, in turn, after examining the animal, telephones his findings to the Health Department and submits a written report. If the animal is or might be rabid, the SPCA is asked to pick it up and keep it in the shelter for examination and observation by a Health Department veterinarian. If the animal is rabid or probably rabid, these observations are telephoned to the main office, which makes arrangements for a Health Department physician to go to the home of the person bitten to give the first antirabies vaccine, with treatment to be given in the Anti-Rabies Clinic for the next 14 days.

The Police Department serves summonses to violators of any rules of the health code pertaining to the care of animals. The "Health Squad" of the Health Department, composed of four policemen, follows up delinquent cases (people who don't answer the summonses). The Sanitation Department picks up and disposes of dead dogs, especially those killed by accident on the street. A biting dog that dies is transferred to the Health Department laboratory for diagnosis. The Sanitary Division of the Health Department checks on complaints of nuisances created by dogs which are permitted by their owners to roam at large. They also inspect pet shops for sanitation and report the presence of sick animals to the Veterinary Division of the Health Department. Pet shop owners are required to keep records as to the origin of animals, purchasers' names and addresses, and other pertinent information so that in case of rabies, we can trace the animal's history.

The Department of Health, Bureau of Laboratories, examines all biting animals that die during the 10-day observation period. The rabies laboratory expert technicians check for:

1) Negri bodies
2) Fluorescent antibody test
3) Mice inoculation

Their early reports are important in the follow-up and disposition of each case.

The SPCA in New York City is a quasi-official organization functioning under a state law enacted in 1894, which grants the society the right to issue dog licenses and use the proceeds to care for stray animals in the city and carry out other humane activities (Table 2). There are about 300,000 dogs licensed in New York City. The license fee is $5. This affords the SPCA sufficient income to pay for the elimination of strays. The society cooperates with the Health Department in all functions relating to rabies control programs.

There are five shelters where Health Department veterinarians examine biting animals. Animals detained for observation are kept by the SPCA. Animals ordered destroyed by our veterinarians are killed painlessly and the carcasses disposed of. Dead animals held for our laboratory are kept under refrigeration during weekends and holidays before being transferred to our laboratories. Stray animals are collected by SPCA trained dogcatchers and carried off in safe delivery vehicles. Shelters are equipped with individual cages to keep animals under observation.

When rabies is found in an area, all strays

Table 2.—*Stray, biting, and rabid animals in New York City—1926-64*

Year	Number of stray animals collected by SPCA	Number of biting animals	Number of rabid animals	Cases of rabies in man	Year	Number of stray animals collected by SPCA	Number of biting animals	Number of rabid animals	Cases of rabies in man
1926...	....	8,611	456	1	1946...	9,600	30,383	113	0
1927...	....	11,490	464	6	1947...	12,200	20,691	47	0
1928...	....	11,683	256	2	1948...	10,500	27,198	26	1
1929...	....	12,279	155	2	1949...	8,100	28,665	0	0
1930...	....	13,322	101	1	1950...	8,200	28,511	1	0
1931...	19,800	14,315	56	0	1951...	6,600	30,107	0	0
1932...	17,500	15,330	18	0	1952...	4,900	28,157	1	0
1933...	13,500	18,307	26	0	1953...	5,800	29,154	2	0
1934...	21,300	20,416	44	2	1954...	8,800	30,494	1	0
1935...	20,500	22,497	20	0	1955...	7,600	29,940	0	0
1936...	24,200	25,111	27	1	1956...	7,000	29,401	0	0
1937...	26,600	25,530	68	0	1957...	6,070	29,625	0	0
1938...	20,500	28,643	86	1	1958...	7,043	29,939	0	0
1939...	27,700	29,683	58	1	1959...	8,026	28,830	0	0
1940...	31,600	28,744	114	2	1960...	8,320	27,137	0	0
1941...	22,100	32,272	31	1	1961...	6,972	26,095	0	0
1942...	14,100	28,854	49	0	1962...	6,961	27,202	0	0
1943...	7,600	24,695	14	0	1963...	7,340	27,976	0	0
1944...	9,500	29,488	34	1	1964...	8,260	30,321	1	0
1945...	8,000	24,815	5	0					

and unleashed animals are picked up immediately and taken to shelters for observation. Daily pick-ups are made from then on by raid wagons until the emergency is over or quarantine lifted. Unclaimed dogs are destroyed. Others are released to owners after a period of observation and proof of rabies vaccination within a 12-month period; otherwise, the dog is vaccinated and kept for 3 months under observation before being released. Should the owner object to vaccination, the animal is kept for a 6-month quarantine period. No dogs from suspected areas are given for adoption. Vaccination of dogs is done by private veterinarians at the owners' expense. Quarantine of animals is permitted at private veterinary hospitals, also at the owners' expense. Rabies-suspect animals must be surrendered to the Health Department and kept under observation.

The veterinary association could be of help in cases of emergency or in vaccination programs. To date, this association has not yet been called upon, as an organized group, to assist in a rabies control program.

Until 1958, all biting animals were examined by Health Department veterinarians. An amended law permits private veterinarians to examine biting animals and report their findings to the Health Department. Any questionable case is sent to a Health Department shelter to be kept under observation.

All biting animals must be examined as soon after the bite as possible and again in 10 days. In the case of face bites, the animal is detained for the 10-day observation period. No inoculations whatsoever are permitted during the observation period.

Vaccination of animals is voluntary and is carried on by private veterinarians. Chick embryo (LEP) vaccine every third year or phenolized tissue vaccine annually is recommended for dogs and only phenolized tissue vaccine for other animals.

Before schools close and during the time when people plan vacations in the country, where dogs are permitted to run loose and may be bitten by a rabid fox or skunk, pet owners are advised by radio, newspapers, and television to re-vaccinate their pets before leaving the city.

Post-exposure treatment of man by the Health Department follows the recommendations of the World Health Organization. The use of duck embryo vaccine was adopted in 1959 after many years' use of Semple vaccine (since 1913). Health Department records report the use of of Pasteur treatment from 1898, with some modification in the preparation of the vaccine, until the Semple phenolized vaccine replaced it. As the use of antirabies vaccines increased, the fear of post-vaccinal encephalitis increased. Since the introduction of the duck embryo vaccine, we have had only two cases of severe reaction directly attributable to the vaccine.

During the years 1935-1951, when rabies was prevalent in the city, every person bitten on the

Table 3.—*Antirabies treatment given at New York City Health Department antirabies clinics*

Year	Number of injections given	Number of persons treated
1935	17,347	1,529
1936	18,624	1,774
1937	21,293	1,988
1938	26,405	2,504
1939	23,921	2,725
1940	22,272	2,474
1941	21,546	2,721
1942	21,518	2,813
1943	17,143	2,277
1944	22,514	3,125
1945	20,556	2,637
1946	28,856	3,452
1947	23,742	2,844
1948	21,088	2,692
1949	19,230	2,614
1950	17,633	2,501
1951	14,339	1,855
1952	8,415	823
1953	8,592	775
1954	5,561	560
1955	5,240	491
1956	4,518	433
1957	3,944	367
1958	4,275	380
1959	3,660	344
1960	2,455	282
1961	3,111	277
1962	3,975	362
1963	3,842	318
1964	3,947	346

Source: Bureau of Preventable Diseases, Div. of Epidemiology and Diagnosis.

face was given seven injections until a decision of "not rabid" was reached on the biting animal (See Table 3).

A person bitten by a stray dog is advised to take the series of injections. About 10 percent of dog bites are by strays, whose owners cannot be traced. No injections are recommended for stray-cat bites as we have not had a rabid cat since 1948. The reason for continuing to recommend treatment after exposure to stray dogs is that there still is rabies in the state, and it is on the increase.

No hyperimmune serum has been used by the Health Department, because the fear of horse serum reaction is greater than the possibility of contracting rabies.

Public relations through the newspaper, radio, and television media should be carried on continually. Individuals and the public in general become panicky when threatened with rabies. Panic should of course be avoided for better cooperation by all concerned.

In 1940, at the height of the rabies epidemic in New York City, the "Eagle," a Brooklyn newspaper, carried adverse publicity implying that there was no rabies, that people should not fear dog bites and not take the antirabies treatment. This contention cost the life of a Brooklyn high school teacher who was bitten by his own dog. The Health Department had advised treatment when our veterinarian had declared the dog rabies suspect. The dog died, and the laboratory report was positive (Negri bodies were found). This was the last case of rabies in a human in New York City.

In summary: Control of rabies is maintained in New York City by strict and constant vigilance by the Health Department with a definite set of laws to be observed by dog owners and enforced by the Police Department. They call for:

1) Examination by veterinarians of all biting animals.
2) Pick-up of all stray dogs and cats from city streets.
3) Maintenance of well equipped animal shelters, with kennels and trained personnel.
4) Close check on all ports of entry.
5) Maintenance of efficient laboratories with technicians who are well trained in microscopic, fluorescent antibody, and mice inoculation techniques.
6) Vaccination of all dogs periodically.
7) Treatment to protect humans exposed to rabies.

Discussion--Urban Rabies Control
Use of Immune Serum in Cats in Quarantine

John Micuda, D.V.M.[1]

Quarantine and observation of biting animals is probably the most accurate method of determining if the animal did have virus in its saliva at the time of the bite and if the person bitten was exposed to rabies. If the animal dies of any disease during the quarantine period, it is then necessary to process its head as though the animal had never been held for observation, and the purpose of the quarantine is defeated. This is an account of how we were able to reduce the numbers of deaths in cats in quarantine due to diseases other than rabies.

The mortality rate of quarantined cats was reduced from a high of 20 percent to less than 3 percent by the use of hyperimmune serum from the blood of cats that had survived 14 days of quarantine and were in good condition at the time of bleeding. Frequently 2-to-3-year-old male cats (strays) in good physical condition were bled and the blood pooled with the blood of donors that had passed quarantine.

It was estimated that 20 to 25 percent of all cats quarantined at our center were either visibly sick or in the incubative stage of disease and that the rest would certainly be exposed before the end of their quarantine period. Therefore, all cats were given 3 to 6 cc of serum upon entrance, and this dosage was repeated in 7 or 8 days, or sooner if the cat was seriously ill. Vitamin B complex with vitamin C and 5 percent dextrose was used in those cases showing severe dehydration. All treatment was by subcutaneous injection. No oral medication was attempted except under unusual circumstances, and then only by myself (orally—penicillin 300,000 units with trisulfa tablets, 1 B.I.D., very good.) Although our personnel were permitted to give injections, oral medication was prohibited. Neoprontosil in doses of 1 to 3 cc is recommended in severe cases of enteritis. All treatment of sick animals is done by or under direct supervision of veterinarians.

Blood donors, after 14 days quarantine, are given enteritis vaccine to increase the antibody content of their blood before bleeding.

During the manufacture of hyperimmune serum, one must always keep in mind that the value of hyperimmune serum is in direct proportion to the immunity of the donor from which the serum is made.

We make fresh serum every 10 to 12 weeks. It is recommended that a minimum of five blood donors be bled at one time and this serum pooled before processing. Occasionally whole blood may be desired for intravenous use in the anemic cat to combat babesiasis or other red blood cell destroying organisms. Pooled citrated blood in 20 cc doses may be given intravenously and repeated in 24 to 48 hours, as the need exists.

Donors are all anesthetized, using a combination of one-half surital (thiamylal sodium) and pentobarbital sodium, mixed together in syringe and given very slowly intravenously using a 25 gauge 1/2-inch needle and a 2-1/2 or 3 cc syringe until eye reflexes are absent. The dose needed may vary from 1-1/2 to 2-1/2 cc. All donors are anesthetized at one time and an area over the left chest closely clipped of hair, scrubbed, and painted with suitable antiseptic. Each donor is then bled out by heart puncture, and either gravity flow or vacuum bottle may be used. The blood is permitted to clot, and serum is removed and pooled. The freshly pooled serum is centrifuged, and the supernatant clarified by serial filtration. Final filtration is through a membrane filter with a pore size of 0.45 microns. Penicillin potasium "G" crystals, 600,000 units, are disolved in 3 cc physiological saline and mixed with streptomycin crystals, 2.5 grams, dissolved in 6 cc physiological saline. This mixture is then added to 100 cc of serum as preservative. Serum is stored in an ordinary refrigerator until it is used or a new supply is prepared.

[1]Quartz Mountain Animal Hospital, Scottsdale, Arizona.

California State Rabies Control Program

George L. Humphrey, D.V.M.[1]

Adequate programs of canine rabies control at the state level have only begun to be realized in recent years, in reality since the availability of a safe, proven immunizing agent against the disease: chick-embryo origin low egg passage (LEP) Flury strain rabies vaccine (11, 18). The control program implemented in California in 1957-1958, based on legislation adopted by the 1957 state legislature, is one such program made possible by chick-embryo (LEP) Flury strain rabies vaccine. Without the commercial availability of such an immunizing agent, legislation could not have been passed, and the program of canine rabies control which exists today would not be possible. It is the purpose of this paper to examine what has been accomplished in the control of canine rabies in California since passage of the 1957 law. California experience may have some applicability in other states having a rabies problem.

It is not known how long rabies has been present in California. However, the book, John Marsh, Pioneer, makes reference to the occurrence of canine rabies and to cases of hydrophobia in man being cared for by Marsh, the first American to practice medicine in California, in Los Angeles in 1836 (12). So great was the menace of rabid dogs at the time in Los Angeles, that a decree was passed by Mexican officials "that no man should keep more than two dogs and that both should be securely tied. The others were poisoned."

The earliest reference to wildlife rabies in California was published in May 1874; the author makes reference in a footnote to a disease in man like hydrophobia following bite by the spotted skunk, Spilogale putorius (8).

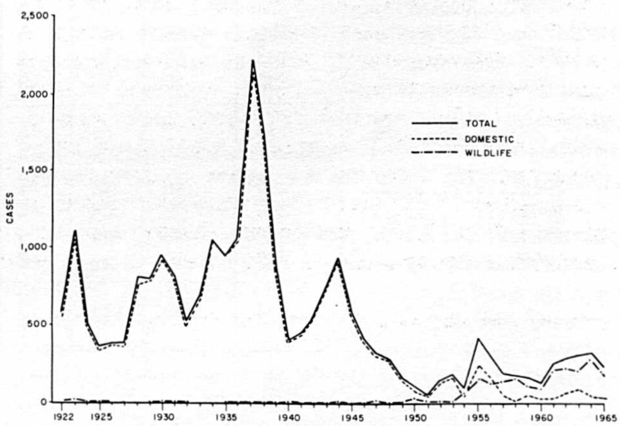
In 1898, an outbreak of dog rabies of short duration occurred in Los Angeles (1). The outbreak was followed by a human rabies death in 1899. One of the 1898 canine cases and the human case were confirmed by animal inoculation. These 2 cases were the first laboratory confirmations of rabies in California (1). Another small outbreak of dog rabies of short duration occurred southwest of Los Angeles in 1906. No other cases were recorded until 1909 (1).

In June 1909, another outbreak of rabies in dogs began in Los Angeles (1). The problem in Los Angeles had largely subsided by early 1910; however, this outbreak was the origin of an epizootic of canine rabies which by March 31, 1913, had spread throughout California from the Mexican Border to the Oregon State Line and affected 31 of the 58 counties (6, 15) California has been continuously affected by rabies since June 1909, a total of 57 years as of June 1966.

From 1909 through 1953, except for the period 1915-1917, when a widespread epizootic of coyote rabies affected northeastern California and the adjoining areas of Oregon, Nevada, and western Utah (2-5, 13-14), rabies in dogs constituted the chief problem in California, and wildlife were little involved (Figure 1).

In 1913, the state legislature adopted a rabies control law which provided for the establishment of rabies quarantines by the State Department of Public Health, the right-of-entry upon private property for purposes of enforcement, and authority to kill dogs found at large as well as other related powers (17). The provisions of the law

Figure 1.—*Cases of animal rabies California, 1922-1965*



Source: State of California, Department of Public Health, Morbidity Records.

[1]Head, California State Rabies Control Program, Veterinary Public Health Section, Bureau of Communicable Diseases, California State Department of Public Health, Berkeley, California.

adopted in 1913, while later augmented, remain in effect and are unchanged today. Despite the broad authority provided by the 1913 legislation and vigorous enforcement carried out in California for many years, canine rabies continued to occur as a series of local epizootics rarely affecting any one locality for more than a few years. An exception to this was Los Angeles County, where dog rabies remained a continuous problem until brought under control in 1957.

In 1950, a change in the occurrence and distribution of rabies in California began to occur. Slight increases in the number of cases of rabies in wildlife, principally skunks and foxes, were noted in certain areas. This increase in incidence of wildlife cases of the disease continued through 1953 (Table 1). There was no apparent correlation between the increased incidence of rabies noted in wildlife and the distribution of the disease in dogs.

Table 1.—*Cases of animal rabies—Annual totals, cases in dogs and other domestic species, cases in wildlife, and number of counties reporting, California, 1950-65*

Year	Total cases all species	Cases of rabies in domestic species: Cases of rabies in dogs: Total dogs	In Mexico border area[1]	In balance of state	Other domestic species (excluding dogs)	Cases of rabies in wildlife: Total wildlife cases	Skunk	Bat	Other wildlife species	Number of counties reporting cases: Total counties reporting rabies	In dogs	In wildlife, all species	In skunks	In bats
1934-1949	12,562	11,642	....	....	842	78	16	0	62	50	47	18	8	0
1950-1965	3,359	1,089	315	774	237	2,033	1,594	288	151	53	30	[2]53	41	46
1950	111	70	39	31	[3]13	28	14	0	[2]14	13	9	6	4	0
1951	54	33	13	20	9	12	6	0	[3]6	8	4	5	2	0
1952	142	103	21	82	23	16	9	0	[4]7	3	5	9	6	0
1953	174	155	8	147	6	13	6	0	7	16	7	8	6	0
4-year subtotals	481	361	81	280	51	69	35	0	34	26	14	17	12	0
1954	85	34	1	33	7	44	32	1	11	20	9	15	14	1
1955	425	246	0	246	13	166	141	2	23	34	10	31	26	2
1956	302	141	0	141	36	125	119	4	2	32	8	30	29	3
1957	197	49	0	49	8	140	130	2	8	32	6	31	30	1
4-year subtotals	1,009	470	1	469	64	475	422	9	44	42	19	41	40	6
1958	173	4	0	4	8	161	145	8	8	34	3	34	32	5
1959	166	34	29	5	20	112	82	18	12	36	5	33	29	10
1960	123	14	10	4	11	98	83	12	3	37	6	35	25	11
1961	253	20	15	5	16	217	174	34	9	41	6	40	33	15
4-year subtotals	715	72	54	18	55	588	484	72	32	46	12	46	37	29
1962	293	46	45	[5]1	22	225	189	29	7	41	3	37	34	15
1963	306	86	84	2	12	208	145	53	10	42	4	41	29	20
1964	328	36	34	2	12	280	208	53	19	41	4	40	28	21
1965	227	18	16	2	21	188	111	72	5	34	4	38	23	23
4-year subtotals	1,154	186	179	7	67	901	653	207	41	51	8	50	36	39

[1]Mexico border area: Imperial and San Diego counties.
[2]Includes 1 case reported in hamster—probably not rabies.
[3]Includes 1 case reported in gopher and 1 in squirrel—probably not rabies.
[4]Includes 3 cases reported in gophers—probably not rabies.
[5]Dog in Butte County developed rabies 5 days after return from 7-week stay in Mexico.

Source: State of California, Department of Public Health, Morbidity Reports CD-77.

During 1954, the 44 cases of rabies reported in wildlife constituted 52 percent of the total of 85 cases of animal rabies reported in the state. The 1954 increase in wildlife rabies in California has continued through the subsequent years with even greater numbers of sylvatic cases being reported (Table 1).

In 1952, the State Department of Public Health drafted legislation with the help of a departmental appointed advisory committee to provide more adequate rabies control measures for the state. When the proposed legislation was introduced into the 1953 state legislature, there was an all-out battle, complete with the playing of "How Much is that Doggie in the Window" on the assembly floor. The antivivisectionists and antivaccinationists prevailed, however, and an amended version of the bill died with the end of 1953 legislative session. Another attempt to secure new legislation was not made until 1957.

During 1955, the California State Department of Public Health, faced with an unprecedented increase in cases of wildlife rabies, added regulations supplementing the 1913 rabies control statutes which provided for declaring counties rabies endemic areas (16). The initial declaration of 26 rabies affected counties in California as rabies endemic areas was made on October 10, 1955 (9); it included all counties that had reported cases of rabies since January 1, 1955. The new regulations made it mandatory for all local health officers in declared rabies endemic areas to establish rabies quarantines within their respective jurisdictions to remain in effect for 365 days after the last reported case of rabies. Rabies endemic areas were defined in the 1955 regulations as "any area . . . where rabies is reported as occurring currently or has occurred within the past 12 months."

In connection with the program, the State Department of Public Health formulated a policy of accepting as a substitute for the required quarantine the adoption and enforcement of an ordinance by a city or county providing for (1) registration of all dogs, (2) maintenance of a pound and pick-up system, and (3) antirabies vaccination of all dogs allowed to run-at-large.

The last declaration was made on September 26, 1957. The rabies endemic area program lasted from October 10, 1955, through December 1, 1957. During that time, a total of 40 rabies-affected counties were declared rabies endemic areas; 13 counties and 120 cities adopted ordinances requiring vaccination of dogs against rabies to avoid being placed under quarantine. Prior to the initial declaration of rabies endemic areas in October 1955, only 9 counties and 55 cities required vaccination of dogs against rabies by local ordinance (9). The status of counties as rabies endemic areas was replaced by declarations as rabies areas effective December 2, 1957, under provision of new statutes added by the 1957 state legislature.

In 1956, the California State Chamber of Commerce organized a rabies committee, consisting of representatives of 17 statewide organizations and official agencies (9), which drafted proposed rabies-control legislation that was ultimately adopted by the 1957 state legislature. The new 1957 law added Sections 1901.2, 1920, and 1921 to the California Health and Safety Code, as follows:

"Section 1901.2. Rabies area shall mean any area not less than a county as determined by the director within a region where the existence of rabies constitutes a public health hazard, as found and declared by the director, after consultation with, and the approval of, the regional advisory committee. A region shall be composed of two or more counties as determined by the director. For each such region there shall be an advisory committee. The regional advisory committee shall consist of nine persons which shall include a health officer, a representative of the medical profession, a veterinarian, the mayor of the city having the largest population in the area, the chairman of the board of supervisors of the county having the largest population in the area, and such representatives of the livestock industry, civic, dog owning, and humane groups as may be appointed by the director to serve without compensation, but shall be reimbursed for actual and necessary expenses incurred during service on the committee. The status of an area as a rabies area shall terminate at the end of one year from the date of the declaration unless, not earlier than two months prior to the end of such year, it is again declared to be a rabies area in the manner provided in this section. If however, the director at any time finds and declares that an area has ceased to be a rabies area its status as such shall terminate upon the date of such declaration.

"Section 1920. In rabies areas:

"(a) Every dog owner, after his dog attains the age of four months, shall annually secure a license for said dog. License fees shall be fixed by the responsible city, city and county, or county, at an amount not to exceed limitations otherwise prescribed by state law or city, city or county, or county charter.

"(b) Every dog owner, after his dog attains the age of four months, shall at such intervals of time not more often than once a year as may be prescribed by the department procure its vaccination by a licensed veterinarian with a canine antirabies vaccine approved by and in a manner prescribed by the state department.

"(c) All dogs under four months of age shall be confined to the premises of, or kept under physical restraint by, the owner, keeper, or harborer. Nothing in this chapter shall be construed to prevent the sale or transportation of a puppy four months old or younger.

"(d) Any dog in violation of the provisions of this article, and such additional provisions as may be prescribed by any local governing body, shall be impounded as provided by local ordinance.

"(e) It shall be the duty of the governing body of each city, city and county, or county to maintain or provide for the maintenance of a pound system and a rabies control program for the purpose of carrying out and enforcing the provisions of this section.

"(f) It shall be the responsibility of each city, county, or city and county to provide dog vaccination clinics, or to arrange for dog vaccination at clinics operated by veterinary groups or associations, held at strategic locations throughout each city, city and county, or county. The vaccination and licensing procedures may be combined as a single operation in such clinics. No charge in excess of actual cost shall be made for any one vaccination at such clinic. No owner of a dog shall be required to have his dog vaccinated at a public clinic if the owner elects to have the dog vaccinated by a licensed veterinarian of the owner's choice.

"Section 1921. Nothing in this chapter is intended or shall be construed to limit the power of any city, city and county, or county in its authority in the exercise of its police power or in the exercise of its power under any other provisions of law to enact more stringent requirements, to regulate and control dogs within the boundaries of its jurisdiction."

The chief problem with rabies control in California prior to 1958 was the lack of adequate local control programs. While many cities and counties maintained and enforced adequate control measures, many neighboring cities and counties did not. These latter jurisdictions weakened and nullified rabies control in the state by abstaining from enactment and enforcement of needed control measures. The purpose of the 1957 rabies-control legislation was to provide adequate local control and enforcement by establishing minimum standards for such programs and to provide a mechanism whereby the requirements of the law can be applied to rabies affected areas of the state.

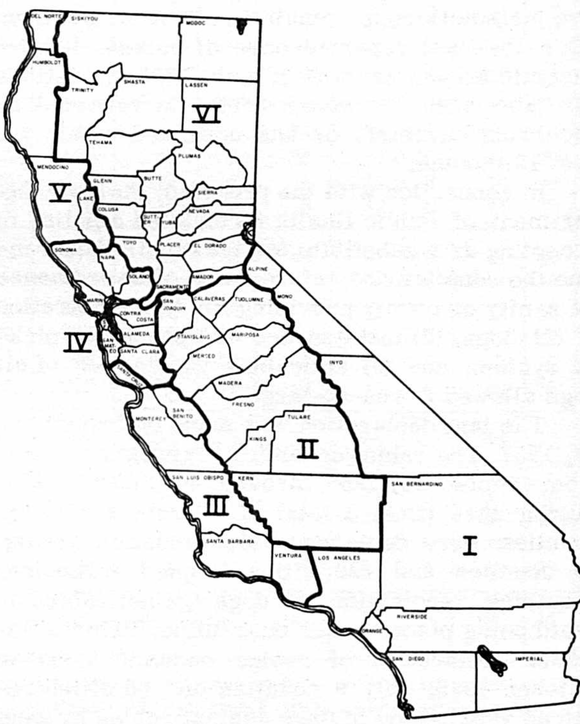
In implementing the new law, the State Department of Public Health divided the state into six rabies regions (Figure 2) and appointed a nine-member rabies advisory committee for each (9). During the period September 13-November 8, 1957, an initial combined meeting of all six regional rabies advisory committees was held, followed by individual meetings of each of the advisory committees within their respective regions. In the course of the latter individual meetings, the six advisory committees formally approved the declaration of 31 counties as rabies areas, effective December 2, 1957 (9).

To implement the new law, the California State Board of Public Health adopted revisions in rabies regulations on December 13, 1957, which became effective January 18, 1958. Those portions of the 1958 regulations affecting the administration of local control programs in declared rabies areas remain unchanged and are included under Section 2606.4, Title 17, California Administrative Code as follows:

"Section 2606.4. Officially Declared Rabies Areas. (a) Administration and Enforcement. For purposes of administration and enforcement of Section 1920, California Health and Safety Code, in officially declared rabies areas, the following shall apply:

"(1) Licensing and Vaccination Procedure. The vaccination of dogs four months of age or older as required by subdivision (b), Section 1920, California Health and Safety Code, shall be held a requisite to licensing as required under subdivision (a) therein. Completion of the licensing procedure consists of issuance of license and vaccination tags or vaccination tag bearing the license data and shall be carried out only after presentation of a valid official vaccination certificate indicating that the period of time elapsing from the date of vaccination to the date of expiration of the license being issued does not

Figure 2.—*California's rabies regions*



ESTABLISHED BY THE CALIFORNIA STATE DEPARTMENT OF PUBLIC HEALTH UNDER PROVISIONS OF SECTION 1901.2 OF THE CALIFORNIA HEALTH AND SAFETY CODE exceed 30 months in the case of vaccination with chick-embryo rabies vaccine or 18 months in the case of vaccination with nerve-tissue rabies vaccine.

"(2) Interval Permitted for Procurement of Vaccination and Licensing. The vaccination of dogs four months of age against rabies as required under subdivision (b), Section 1920, California Health and Safety Code, and the license required by subdivision (a) of said section shall be procured not later than 30 days after the dog attains the age of four months. The annual renewal of licensing as required under subdivision (a) of said section and revaccination as may be required under subdivision (b) of said section shall be procured not later than 60 days after expiration of the previously issued license.

"(3) Rabies Control Activities Reporting. During such time as a county is under official declaration as a rabies area, each local official responsible for the various phases of local dog or rabies control within each city, county and city or cities, or county shall make quarterly rabies control activities reports to and on forms furnished by the department. Such reports shall be submitted to the department by the local officials responsible for the various phases of local dog or rabies control through the local health officer so as to reach the department no later than 30 days following each quarter.

"(b) Vaccination of Dogs Against Rabies. Dogs shall be considered to be properly vaccinated for the purposes of Section 1920, California Health and Safety Code, when injected at four months of age or older with canine chick-embryo origin modified live-virus rabies vaccine or canine nerve-tissue killed-virus rabies vaccine in a manner prescribed by the department.

"Dogs receiving INITIAL injection of rabies vaccine shall be confined to the premises of, or kept under physical restraint by, the owner, keeper or harborer until 30 days have elapsed following vaccination."

Certain provisions of the law and regulations are of particular import and should be emphasized: (1) the law places direct responsibility for maintaining or providing for a pound system and a rabies control program for the purpose of carrying out and enforcing the law upon the boards of supervisors and city councils, (2) regulations adopted by the State Board of Public Health require that local enforcement authorities hold vaccination requisite to licensing, and (3) regulations require the reporting of local rabies control activities by each control jurisdiction within declared rabies area. Without the foregoing requirements, the effectiveness of the 1957 law to a large degree would be nullified.

The vaccination requirements of the law do not constitute a hardship upon the dog owner. The law provides for the holding of low-cost public vaccination clinics. The usual fee for vaccination in these clinics is $1.50 to $2.00. Chick-embryo vaccine which is accepted for a 2-year period under state regulations constitutes the vast majority of vaccine used in the state and costs the dog owner attending clinics an average of $0.75 to $1.00 annually.

From implementation of the law on December 2, 1957, through December 31, 1965, a total of 315 declarations have been made designating a total of 48 of the 58 counties in California rabies areas. As of December 31, 1965, 35 counties were under declaration as rabies areas.

During the 9-year period 1956-1964, a total of 5,394,068 doses of canine rabies vaccine were distributed in California by the various manufacturing biological firms. Of the foregoing amount, 4,955,321 doses (92 percent) were chick-embryo type. During 1964, a total of 865,879 doses of rabies vaccine were distributed in California, 815,580, over 94 percent of which was the chick-embryo type.

During the last 5 years, 1961-1965, an average of 837,000 dogs were reported licensed annually in counties declared rabies areas. An average of 379,700 dogs were reported impounded annually during the same period, of which nearly 256,000, or approximately 64.7 percent, were reported destroyed. As of January 31, 1966, 47 (81 percent) of the 58 counties in California had passed ordinances requiring vaccination of dogs against rabies and of the 386 incorporated cities, 293 (76 percent) require vaccination against rabies.

The implementation and administration of a rabies control program from the state level in an area such as California is complicated by a multiplicity of local government jurisdictions varying from concentrated urban to sparsely populated rural areas. The program is additionally complicated by the wide variety and number of local government agencies and officials having responsibility for dog control and licensing. City and county tax collectors and city and county clerks are involved in many areas with the collection of dog license fees. City and county pounds are administratively responsible to city councils or boards of supervisors or to local health departments, the county sheriff, city and county administrators, county agricultural commissioners, and county veterinarians. In addition, many county pounds are serving cities through contract, counties are contracting with cities for pound facilities, and humane societies are serving cities and counties via contract. All are concerned with license sales, stray-dog control, and pound operation dependent upon the varying patterns which may exist in a particular jurisdiction. Local health departments, veterinarians individually or as organizations or groups, together with various enforcement agencies and in some cases volunteer organizations are concerned with the holding of low cost public rabies vaccination clinics. Last, but not least, city councils and county boards of supervisors are concerned with the adoption of local ordinances, setting of policy, and appropriation of funds for local program operation.

The role of the state is to administer the law, not enforce it. In addition to such administration, the Department of Public Health carries out rabies activities not associated with the administration of control statutes. At the present time approximately 0.7 of the time of one veterinarian and 0.75 of one clerk's are spent on rabies activities of the Department, including administration of the control law. Two forms are currently being used which greatly reduce the amount of time spent in administering the law. The first of these is the so-called "Statement of Enforcement" form (CD-2772) which is utilized to secure acknowledgement from the governing bodies affected by the declarations of rabies areas of the fact of declaration and to assure that they are complying with the provisions of the law (Figure 3). The second form is the "Quarterly Report of Local Rabies Control Activities" (CD-1922), used to ascertain that enforcement is being carried out during the period under declaration as a rabies area (Figure 4).

The primary objective of the California rabies control program is the prevention of canine rabies. With any program of control or prevention which has been in effect for a significant period, there comes a time when the question of how effective the program has been in achieving its objective must be answered. The most direct means of evaluation in a program of this type is to observe what has occurred before and after implementation of the program in question. The figures included in Table 1 provide some insight into this question regarding the California program.

From 1909 through 1953, the California problem consisted primarily of rabid dogs, with the one exception of the period 1915-1917, when an outbreak of coyote rabies involved northeastern California. This outbreak, however, was confined to the east side of the Sierra Nevada range (9). The figures on reported cases of rabies during the 16-year period 1934-1949 typify the rabies problem in California during the period 1909-1953 (Table 1). During the 16-year period 1934-1949, a total of 12,562 cases of rabies were reported in California, 11,642 (92 percent) of which were in dogs. Only 78 (0.6 percent) occurred in wildlife during the same period. The years 1950-1954 represent a transition period during which the annual incidence of wildlife rabies gradually increased. By 1958, canine rabies as a problem in California was

Figure 3.–*State of California Department of Public Health*

Statement of Enforcement of Rabies Control Requirements for *Rabies Areas* Applying to

________________ **Effective** ________________
(County) (Date)

____
Area or Jurisdiction for Which Statement is Made

Statement Completed By:	**Endorsement by Local Health Officer or Authorized Representative:**
Date	Date
Signature	Signature
Name (print)	Name (print)
Title	Title
Address	Local Health Department

1. Licensing required? Yes ☐ No ☐ AGE at which licensing required ______
2. Vaccination required? Yes ☐ No ☐ If yes, answer a and b below.
   a. As a requisite to licensing? Yes ☐ No ☐
   b. By local ordinance? Yes ☐ No ☐
3. Dog pound maintained? Yes ☐ No ☐ If yes, answer a and b below.
   a. Government owned? Yes ☐ No ☐
   b. Contract with ______
4. Dogs under four months required to be kept confined to the premises of owner, keeper or harborer? Yes ☐ No ☐
5. Impound stray unowned dogs and those in violation of provisions of Section 1920, California Health and Safety Code, and 2606.4, California Administrative Code. Yes ☐ No ☐
   a. Government employed enforcement personnel? Yes ☐ No ☐
   b. Contract with ______
6. Provide or arrange for low cost rabies vaccination clinics? Yes ☐ No ☐ If yes, answer a and b below
   a. Number of clinics held per year ______
   b. Vaccination fee charged at clinics ______

(See Reverse for Instructions)

COMPLETED FORM TO BE SENT DIRECTLY TO THE LOCAL HEALTH OFFICER (Rev. 2-18-66) Form CD-2772

Figure 4.–*Quarterly report of local rabies control activities*

AREA FOR WHICH REPORT IS MADE: (On county reports, indicate if report covers only unincorporated area. Please list cities served by contract or other arrangement.)

REPORT FOR QUARTER: (Check one)
☐ January - March
☐ April - June
☐ July - September
☐ October - December

		Please add numbers to subtotals and totals; if report for any item is "none" or "zero", so indicate.	NUMBER THIS QUARTER
VACCINATION PROGRAM		A. Dogs vaccinated, TOTAL:	
		1. In low cost public vaccination clinics	
		2. Private vaccinations	
		B. Number of low cost vaccination clinics	
		C. Vaccination fee charged in low cost vaccination clinics $ ______	
CANINE RABIES CONTROL	Registration	D. Number of dogs licensed	
		E. Dogs licensed for which valid vaccination certificates were submitted	
	Stray Dog Control	F. Dogs impounded	
		G. Dogs redeemed	
		H. Dogs sold or given away	
		I. Dogs destroyed	
	Enforcement	J. Warnings issued for violations, vaccination and/or license requirements of State law or local ordinance provisions	
		K. Number brought to court	
		L. Convictions obtained	
ANIMAL BITES REPORTED		M. Animal bites reported, TOTAL:	
		1. Dog bites reported, Total:	
		a. Licensed and vaccinated	
		b. Licensed only	
		c. Vaccinated only	
		d. Neither licensed nor vaccinated (but owned)	
		e. Neither licensed nor vaccinated (strays)	
		2. Other animal bites reported, Total:	
		a. Domestic	
		b. Wild	
ADMINISTRATION		Name of agency or organization responsible for direction of dog control	
		Address	

Signature ______ Agency ______

Title ______ Date ______

State of California
Department of Public Health

(Rev. 11-15-64)
Form CD-1922

largely resolved. However, the incidence of rabies in wild animals has increased tremendously, particularly since 1955.

From 1950 through 1965, a 16-year period, a total of 3,359 cases of rabies were reported in the state, 1,089 (32.4 percent) of which were in dogs and 2,033 (60.3 percent) in wild species. In considering the question of the effectiveness of the California program for prevention of rabies in dogs, it is of interest to examine these 1,089 canine cases and observe when, where, and why they occurred.

For convenience, an annual breakdown of cases is shown in Table 1. Of the total of 1.089 cases of rabies reported in dogs during the last 16 years, 831 (76.4 percent) occurred during the 8-year period 1950-1957. During the subsequent 8 years, 1958-1965, a total of 258 cases of rabies were reported in dogs. It is these latter 258 cases with which we are primarily concerned in evaluating the effectiveness of the present state program for preventing rabies in dogs.

Of the 258 cases of canine rabies reported in California during the last 8 years, 1958-1965, 233 (more than 90 percent) occurred in the immediate area of the California-Mexico Border as compared with only 25 cases in the rest of the state. During the last 4 years, only 7 cases of dog rabies have been found outside of the Mexican Border area, 1 of which, a case in a Butte County dog, developed 5 days after the dog returned from a 7-week stay in Mexico (Table 1).

Ample opportunity exists in California for dogs to be exposed to rabies. The disease in wildlife has been widespread since 1954. Of the total of 3,359 cases of animal rabies reported during the past 16 years, 2,033 (more than 60 percent) have been in wildlife species. Of these 2,033 wildlife cases, 1,489 (more than 73 percent) have been reported during the last 8 years. The vast majority of wildlife cases have been found in skunks, nearly 78 percent of the total in wild species and nearly 48 percent of all species reported rabid in the state since 1950. Cases of rabies in bats have constituted an increasingly greater proportion of the total since the first rabid bat was found in California in 1954 (Table 1). Rabies infection in wildlife has been reported from all of the 53 counties reporting cases of rabies in California since 1950. Rabid skunks have been found in 41 counties since 1950 and rabid bats in 46 counties since 1954.

The reduction and prevention of canine rabies infection in all but two California counties (San Diego and Imperial) has occurred in the presence of an exceedingly large reservoir of rabies in wildlife. This fact raises the question of why dog rabies in Imperial and San Diego counties has continued to persist (233 cases since 1959 and 1962, respectively) if California can so successfully prevent the canine disease in the other 56 counties.

The key to the continued persistence of Imperial-San Diego counties' rabies problem is Mexico. Both Imperial County (since 1959) and San Diego County (since 1962) have continuously enforced outstanding programs of rabies control, including unprecedented enforcement of stray-dog control, licensing, and vaccination of dogs against the disease. Both have included measures aimed at reducing the hazard of transmission of rabies from wildlife (coyotes) to dogs.

There is ample evidence that the continuing rabies problem in Imperial and San Diego counties has its source in the uncontrolled occurrence of rabies in dogs in the adjoining areas of Mexico (Tijuana and Mexicali Valley). Of the total of 244 cases of animal rabies (excluding 3 cases in bats) reported from Imperial and San Diego counties since 1959 and 1962, respectively, through 1965, 206 were found less than 5 miles from the Mexican Border, 34 between 5 and 10 miles, and only 4 cases at distances of more than 10 miles.

The above distribution of rabies cases in Imperial and San Diego counties is not consistent with the distribution of the human and hence the distribution of the dog population of either county. Numerous rabid dogs have been shot after crossing the border from Mexico. Figures emphasizing this point are available from the Port-of-Entry, Calexico, Imperial County, where a 24-hour dog guard has been maintained since January 22, 1964, to prevent the entry of stray dogs from Mexicali, Mexico. During the approximately 23-month period—January 22, 1964, through December 31, 1965—a total of 193 dogs were apprehended. Of these, seven were returned to owners in Mexico and 171 were examined for rabies in the laboratory. Of the 171 on which examination was completed, 16 were found positive—approximately 9.4 percent of those examined. At one point in 1964, positive examinations ran nearly 30 percent. Under the conditions that exist along the border, it is remarkable that the above counties have so far succeeded in limiting the rabies problem to the areas adjacent to the Mexican Border.

Summary. Existing legislation in California adopted by the state legislature in 1957 provides minimum standards for local control of rabies in dogs. Program enforcement is maintained by local authorities, in keeping with the best interest of program efficiency. Without state legislation there would exist relatively few local ordinances in California requiring vaccination of dogs against the disease. While statewide compulsory vaccination of dogs against rabies would seem less cumbersome than the present declaration of rabies-affected counties as rabies areas with the necessary holding of 10-12 regional rabies advisory committee meetings per year, present legislation provides an effective program basis

which has enabled local governing bodies to implement efficient programs of control without having to face the protests of the antivivisection/antivaccination minority. The program has proved its worth over the past 8 years of operation, from 1958-1965. The present rabies situation in California wildlife warrants continued application and enforcement of existing legislation and program aimed at preventing the occurrence of the disease in dogs of the state. More adequate control of canine rabies in adjoining areas of Mexico would greatly enhance the effectiveness of control work being carried out in the areas of the state adjacent to the California-Mexico Border.

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Discussion--State Rabies Control Program
Tennessee Control Program
Luther E. Fredrickson, D.V.M.[1]

A long-standing rabies problem caused the Tennessee legislature to create a Rabies Control Service in the State Health Department in 1953. Rabies had taken an annual toll of human life ranging from one death to 11, with only an occasional year of relief within the span of available records. Canine rabies was, and had been, the major problem, but fox rabies was emerging at the time of the legislative action (1, 2). Wild animal rabies control, however, is by law the responsibility of the Game and Fish Commission in Tennessee.

A state-wide vaccination program was developed following the 1953 legislative action. Although the law required that all dogs be vaccinated, few communities had the personnel or the desire to support enforcement activities; consequently, an educational program was necessary to gain the cooperation of dog owners.

Vaccination tags and certificates were furnished the local health departments for use by licensed veterinarians. Clinics were organized and promoted by the local health department in each county. These clinics were serviced by resident, practicing veterinarians, or by practicing veterinarians from neighboring counties in the counties without resident practioners. The veterinarians furnished the vaccine, needles, and syringes, administered the vaccine, and collected a modest fee. Educational material, produced and distributed by the State Health Department, was used by the local health department to inform the community of the clinics, their location, and their importance. Much of the educational material was used in the schools, but radio, television, community meetings, and newspapers were all utilized in the promotional activities.

The vaccination program, promoted by educational measures, achieved the vaccination of 45 percent of the estimated dog population in Tennessee by 1955, and the last human death was recorded in October of the same year (3). Canine rabies cases were reduced below that of foxes by 1956. Since then, dog rabies has been held at a low level in spite of an increasingly serious and continuing problem of rabies in foxes.

[1]Tennessee Department of Public Health, Nashville, Tennessee.

Except for the counties without resident veterinarians, the numbers of dogs vaccinated at the veterinarians' offices for regular fees tend to increase in relation to the dogs vaccinated at the public clinics. These clinics, however, served and continue to serve an important educational function in introducing the dog owner to the service of the veterinarian.

The past year, 1965, was the sixth consecutive year for a sizeable increase in the number of canine rabies vaccinations reported under this program. This new high, 336,152, represents 61 percent of the estimated dog population of the state (4). This total plus the number of dogs vaccinated with the 3-year vaccine in the 2 preceeding years gives Tennessee protection from rabies in 84 percent of the estimated dog population. With the serious wild animal rabies problem, this number of vaccinated dogs has probably kept Tennessee from having a dog rabies epizootic and human rabies cases.

During the year, the demand for educational material by local health departments has exceeded our supply and our budget. Approximately 89,000 pieces of educational material on rabies have been distributed; schools used 1,084 teacher kits during the year; and a coloring book, "Susie and Her Dog," was used in the schools of 38 counties. Apparently, the educational measures have been the main factors in the success of the dog vaccination program. Less than 25 percent of the counties have rabies control officers to enforce the rabies vaccination of dogs. The response of the dog owner has been accepted as the result of the educational program.

This educational program has served well. A broader educational program will serve better. In the past, the program has been geared to informing the public concerning rabies, the need for vaccination, and the location and schedule of clinics. This type of program has limitations: the dog owner develops the attitude that rabies vaccination is his one and only responsibility.

Dogs in modern society are the source of many community problems (5), and with continuing increases in the population, the "canine delinquent" becomes more destructive and a more serious problem. Rabies is not the only public health problem of the dog in modern society. He is the source of other diseases also. He attacks and injures children. Some of these attacks are fatal. He causes minor and major accidents on the streets and highways. Marauding dogs destroy livestock and game.

Modern rabies-control education should teach the total responsibilities of dog ownership. Dog owners accepting and appreciating the full responsibilities of pet ownership do not permit their pets to go unvaccinated. Their dogs do not become "canine delinquents." They support enforcement measures. These educational programs should be directed primarily toward the children. (6) This audience is receptive and will influence the adults in the family better than we can. They are also tomorrow's adults.

This is the type of a rabies-control educational program we hope to develop for the future in Tennessee.

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Discussion--State Rabies Control Program
Illinois Rabies Control Law

Paul B. Doby, D.V.M.[1]

The Illinois Rabies Control Law was passed by the Illinois General Assembly in 1953 and became effective June 1, 1954. Prior to this time, Illinois rabies programs were on a local basis with the exception of state authority to issue area rabies quarantines and provisions under the Public Health Law which required a 15-day quarantine on rabies-suspect animals.

The Illinois law provides that each county shall establish a rabies control program. The County Board of Supervisors is to appoint annually a licensed veterinarian to be rabies inspector. The rabies inspector is authorized to administer the program in his county. He may obtain as many deputy rabies inspectors and non-veterinarian inspectors as necessary. The program is financed by rabies vaccination tag fees. Such fees, established by each individual county, are generally from $.50 to $1.50 per dog.

Some of the principal components of the Illinois law are:

1. Annual vaccination of all dogs not confined at all times in an enclosed area.

2. Dogs are considered officially vaccinated only if vaccinated by a licensed veterinarian and official certificate and tag have been issued.

3. Veterinarian required to submit required tag fee to county treasurer of the county in which the dog owner resides.

4. Any dog running at large and not wearing evidence of inoculation may be apprehended and impounded. Impounded, unvaccinated dogs not redeemed by their owners may be humanely destroyed after 7 days.

5. Rabies suspects and animals which have bitten persons are required to be held under observation by a veterinarian for a minimum period of 10 days.

6. The Department of Agriculture is given broad authority in the event of a rabies epizootic. In such cases, the Department of Agriculture may order:

   a. All dogs and other animals in the locality to be (1) kept confined within an enclosure, or (2) kept muzzled and restrained by a leash composed of chain or other indestructible materials.

   b. That all owners or keepers of dogs or other animals take such prophylactic measures as deemed necessary to prevent the spread of rabies.

   c. Other measures as may be necessary to control the spread of rabies in all dogs and other animals.

In addition to the above provisions of the law, all of the successful county rabies programs rely on a continual educational program. Both the Department of Agriculture and the Department of Public Health are available to county rabies inspectors to aid in educational and administrative aspects.

A few of the successful educational aids are:

1. All news media have been utilized in announcing clinics, and publicizing positive rabies cases and provisions of the law.

2. Presentation of rabies films to elementary school groups followed by distribution of leaflets.

3. Maintaining dog census and notification to owners that dogs are due for annual vaccination.

4. Periodic training sessions are conducted for rabies inspectors, law enforcement officers, public officials, and lay inspectors.

5. Periodically a newsletter is prepared by the Department of Agriculture. This is intended primarily as an educational tool for the lay inspector.

We believe that this law has been a very effective weapon in the control of canine rabies in Illinois. In 1952, prior to enactment of the rabies law, 322 cases of canine rabies were diagnosed. The number of cases of canine rabies declined through 1962, when 8 cases were diagnosed. A gradual increase has occurred since 1962,which parallels a marked increase in reported wildlife rabies, primarily in skunks. In areas where there is an effective canine rabies program but where skunk rabies is a problem, a localized skunk reduction program has been used. While this is not considered to be the final answer to skunk rabies, it does appear to be of some benefit. It demonstrates to the public that those involved in rabies control are concerned with all aspects of rabies, not just vaccination.

An unexplained increase in feline rabies occurred in Illinois in 1965. Eighty cases were

[1]Division of Livestock Industry, Springfield, Illinois.

diagnosed, compared with an average of 12 cases each year for the past 10 years.

As is the case with any law requiring administration, there is a wide variation in effectiveness of the program in various counties. In general, the more effective programs are in the central to northern part of the state. There appears to be one primary reason for the geographic variation in the effectiveness of the program; in southern Illinois there is a higher population of hunting dogs. The concensus among Illinois hunters is that rabies vaccination will affect "the scent." Often in many of these counties several members of the board are also members of the hunting fraternity. In a few counties this has resulted in complete neutralization of the program.

Possibly the most important factor in a successful rabies program is the zeal and the enthusiasm exhibited by the lay inspector. Generally the rabies inspector is a practicing veterinarian and by necessity can devote only a small amount of time to administering the program. The educational aspects are effective in promoting increased vaccination initially but continued high vaccination rates are accomplished only when vigorous enforcement is maintained.

The law provides that owners be prosecuted when their dogs are not either officially vaccinated or confined. Several of our most successful county programs follow the policy of prosecution of the owner of any unvaccinated dog involved in a bite case. Animal bite cases are usually well distributed throughout a county. Therefore, prosecution of owners of unvaccinated dogs involved in bite cases serves to continually remind the public of the provisions of the Illinois rabies law.

In conclusion, I would like to bring out a few comparisons between the California and Illinois programs:

1. The Illinois program is established as a continuous state-wide program.

2. Annual vaccination is required in Illinois irrespective of vaccine used. One of the weaknesses of the Illinois program is the fact that the financial support of the program is dependent on tag fees. To date, this has prevented a change in vaccination requirements. The Department of Agriculture, the Department of Public Health, and the Illinois State Veterinary Medical Association are studying this situation and hope to propose an amendment to the law during this coming session of legislature to permit recognition of vaccination with modified live virus vaccines for a period longer than 1 year. This change must be accomplished without detriment to the financial support of the individual county programs.

The California, Illinois, and Tennessee programs have proven effective in controlling canine rabies. None of these programs, however, is of any benefit in reducing wildlife rabies. I feel that for this symposium to have accomplished any useful purpose, out of it must arise a permanent national rabies committee or council to promote research programs to combat the growing menace of wildlife rabies.

Rabies Control in the United States–Legal Aspects

H. W. Hannah, LL.B.[1]

This will be primarily a discussion of principles. The subject matter has been divided into three parts:

I. Applicable common law principles.
II. The role of statutes, ordinances, and regulations.
III. Units of government and what they can be empowered to do.

I. Applicable common law principles. By common law we mean precedent—court decisions which will be followed (or on occasion over-ruled). Over time these decisions result in established principles about which legal scholars can generalize, disagree, and spin refinements. Legislation may corroborate these principles, leave them untouched, vary their meaning, or render them inapplicable. The discussion that follows concerns those principles that still appear to be operative.

1. Nuisance. It seems well established that a "mad dog" is a nuisance which can be abated by anyone with sufficient nerve and an adequate device. In To Kill a Mockingbird the device was a rifle in the hands of Atticus Finch, attorney-at-law. This right overrides statutory formulae. In Illinois, for example, you can kill a dog unaccompanied by its owner when found in the act of wounding, worrying, chasing, or killing livestock. In case of a rabid dog at large these conditions would not need to be fulfilled. Any animal that poses a sufficient threat justifies abatement. We might say a rabid animal fulfills this condition per se. Likewise, game laws protecting named species and requiring a permit to kill when destroying crops would not be applicable with respect to a rabid wild animal of any kind. Any rabid domestic animal, large or small, could constitute a threat if it escapes confinement and, under proper conditions, could be destroyed by anyone as a dangerous nuisance.

2. Negligence and liability— "scienter." Negligence means fault—failure, in a particular set of circumstances, to act as a "reasonably prudent man." Such failure generally results in liability if someone is damaged. Negligent failure to prevent livestock from escaping from your premises will make you liable for the damage they do to others. But the courts have said that you are liable only for foreseeable damage. If your animals have a contagious disease, but you are not aware of it, you are not liable for transmission of the disease. If you are aware—have knowledge or "scienter"—then full liability may follow. Under common law theory, dogs and cats at large do not constitute negligence. But if one has a rabid dog or cat—or one with any other transmissible disease—and is aware of it, then he is negligent to permit it to be at large and fully liable. If a dog or cat is at large contrary to a statute, ordinance, or regulation requiring confinement or leashing, the owner can be held liable in a civil suit for damages caused, but he still would not be liable for transmission of disease unless he were aware that his dog or cat was diseased—or unless the statutes eliminated scienter.

The statutes themselves vary. One, for example, which simply eliminates the "one-bite" theory and says in effect that you are liable when anyone is bitten by your dog, provided the dog was not provoked, would not eliminate the necessity of proving scienter in case your dog were rabid. But some laws and the regulations adopted under them may go further, particularly when municipalities are trying to combat a serious rabies situation. If, for example, the incidence of rabies is high in a locality and there is a leash law and other supporting ordinances or regulations on confinement in force and one is negligent in not obeying these regulations, he might very well be held liable for the transmission of rabies even though he didn't know his dog was rabid. In this situation the reasoning might be that everyone is presumed to know his animal might be rabid and that since laws and regulations are specifically for the purpose of controlling a serious rabies situation, liability for any damage resulting from one's animal's not being confined according to the law and ordinances would follow.

Generally, I think we can still say the argument is sound—that one must have knowledge of a condition which will injure others before he can be held responsible for injury resulting from the condition. But there may be situations where the implication is so strong that only a special set of

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defensive facts could relieve the defendant. Original negligence on the part of the owner must, of course, be assumed. If a cyclone destroys his kennels or vandals come and damage his premises leaving gates and doors open so animals can escape, he naturally is not liable until he is in a position to do something about it and then fails.

We can perhaps generalize further by saying that scienter, as far as it relates to the character of the dog—that is, whether or not it is a vicious animal—may be constitutionally eliminated by statute and the owner held without proof of knowledge on his part. Scienter regarding a diseased condition of an animal is probably not eliminated by most statutes and probably could not be constitutionally eliminated except in situations such as those described above, where there is a general outbreak justifying certain presumptions. One commentator stated learnedly that you keep an elephant at your own risk. This is no doubt true in more ways than one, but I would still argue that this does not make you liable for the transmission of disease by your elephant, since this is not one of the risks you assume in keeping him. I am sure that this would apply even to elephantiasis—which I am told has nothing to do with elephants.

One city ordinance limited the number of cats to be kept in any one residence to five. I suppose if one kept six cats and one of them damaged a neighbor, negligence per se might be argued. The defense that the damage was caused by the fourth cat rather than the sixth would probably not carry much weight. In one interesting Missouri appellate court case a veterinarian recovered for damages caused by the bite of a rabid dog. The veterinarian had been called to treat the animal. According to the facts, the owner suspected rabies, was holding the dog on a leash, and when the veterinarian's back was turned, the dog leaped on the veterinarian and bit him. Not only does this seem to be the right decision—but also it should be of some consolation to veterinarians.

3. Fear of rabies. There are many facts or conditions about which a court will take judicial notice. This means that the court believes that almost everybody knows about this fact or condition and has a certain attitude toward it. The court simply says we share this attitude. Among the things of which courts have taken judicial notice is the feeling generally shared by mankind that death from rabies is an unpleasant kind of demise and that anyone has a right to fear death from this cause more than he might fear death from some other cause. Accordingly, it has been held that anxiety as to the probability of rabies following a dog bite is an element of damages and should be compensable if the defendant is liable otherwise for the bite of his animal. The measure of damages would be a jury question, but I suppose there would be no argument about recovering for the cost of the series of shots required plus time lost and other measurable factors.

4. Defenses. The initial defense in any negligence case is that the defendant was not negligent or that he has not violated some statute, regulation, or ordinance which it is claimed he did violate. Even though there is negligence or a violation of a statute or ordinance, there can be the further defense that the injury complained of did not result from the negligence alleged or from the violation of the particular statute or ordinance. In one rather interesting case, for example, regulations required shipowners transporting livestock to construct pens so animals could be separated. Such pens were not constructed. During a storm at sea many animals were swept overboard. A suit for compensation for their loss followed, one of the allegations being that if pens had been constructed as required by law, the animals would not have been lost. The defense was that no pens were required to keep animals from being lost but only to keep them from getting disease, and since they didn't get a disease, there was no liability. The court held for the defendant.

But even if negligence can be proved, there may be an adequate defense. Generally this would be contributory negligence, assumption of risk, or provocation. If one provokes an animal to attack him, this will generally be an adequate defense. If the provocation is slight and the negligence of the defendant great, it might not constitute a defense. This is one of the interesting things about the law of torts; nothing is cut and dried. If it were, no one would be happy with the law of torts.

The assumption of risk doctrine would apply primarily to employees or others who have accepted a certain situation or condition as a part of their employment or of their service to the defendant. This is generally an adequate defense unless it can be shown that in the particular circumstance the defendant knew something that the plaintiff did not know, so that although the plaintiff may be presumed to have assumed some risks, he could not have assumed all of them because there were some he did not know about. In an Illinois case a farm employee sued his employer for injury caused by a faulty hitch on a tractor. The defense was that the employee knew about the faulty hitch but continued to work with the tractor. The counter to this was that although the employee knew about the hitch, he was not cognizant of the danger created by it. The court held for the plaintiff saying that this was not a situation in which the assumption of risk doctrine applied. It does not require much imagination to transfer this to the animal field and formulate all kinds of hypothetical situations in which assumption of risk either would or would not be an adequate defense.

Contributory negligence might include provocation but it includes other actions too. It might include playing with an animal when one has been warned not to, failure to heed an owner's warnings about proclivities of the animal, failure to heed a sign, or even failure to take adequate measures which most people would have taken following injury by an animal.

5. Selling diseased animals. The principle is well established that one who sells an animal knowing or having reason to believe it has a communicable disease is liable for the transmission of the disease—not only to the purchaser of the animal, but to anyone who might be injured because of the purchase. In an Illinois case a man sold a hog he knew had been exposed to cholera. The purchaser obviously did not know this. He brought the animal home and turned it out in his pasture. His neighbor's hogs contracted cholera, and it was traced to the purchased animal. The neighbor sued the purchaser's vendor and recovered. This seems like good law and should permit recovery even further down the line of proximate cause than the neighbor of one who purchases from a seller who knows his animal is diseased, provided there is no discovery someplace along the chain which would have enabled one of the intervening parties by taking proper action to prevent further dissemination of disease.

In the law of torts there have been many interesting names coined for defenses which arise after the elapse of time: One is the proximate cause doctrine—that is, was the original act really the cause of the injury complained of by the plaintiff? Another is the last clear chance doctrine—which simply means did someone have a last opportunity to prevent the damage complained of? Regardless of the rules which have been coined and the intriguing refinements which can be introduced, we can simply generalize by saying it is pretty risky to sell a diseased animal unless you can prove you didn't know it was diseased and had no reason to suspect it was diseased—and even then there may be some risk involved if it is sold in violation of some statutory or regulatory requirement regarding testing and the issuance of a health certificate. You might be protected under the proximate cause doctrine—and again, you might not be.

Before chopping off our discussion of the common law principles which seem to apply, let us remind ourselves that the application of the common law is an important consideration despite the volume of statutory and regulatory law with which we are now confronted. This is true for two reasons: One, no amount of statutory and regulatory law can comprehend all the situations which will arise; and two, even statutory and regulatory law must be interpreted.

II. The role of statutes, ordinances, and regulations. The legislative control of rabies is primarily in the domain of the states. Through exercise of the police power the legislature may do a number of things:

1. Require counties or other units of government to carry on a vaccination, tagging, and certification program under which dog owners are compelled to comply.
2. Quarantine.
3. Require confinement.
4. Require leashing or muzzling or both.
5. Require confinement and observation of any animal that has bitten someone.
6. Destroy.
7. Impound dogs running at large contrary to law.
8. Require anyone noting symptoms of rabies in a dog or any other animal or having knowledge of someone who has been bitten to notify the rabies inspector immediately.
9. Tax dogs.
10. Provide for the establishment and maintenance of pounds.
11. Establish a state-wide predator-rabies control program involving the trapping of foxes and other animals—fox hunters to the contrary notwithstanding (witness experience with the Virginia law reported in the JAVMA July 15, 1963).
12. Restrict or forbid entry of diseased or suspect animals into the state.
13. Make human antirabies shots available to physicians free of charge.
14. Establish and support research on rabies.
15. Control the production and distribution of rabies vaccine and of antirabies vaccine.
16. Authorize municipalities to "contract" with appropriate agencies for rabies control.

Laws and ordinances should not become ends in themselves. To achieve effective control or elimination there must be agreed-on objectives and goals. Laws and ordinances should be designed to help achieve these objectives and goals. They should be repealed, modified, or augmented when they are not contributing to the objective.

III. Units of government and what they can be empowered to do. Local government, especially municipalities and counties, play an important role in rabies control. Perhaps the nature and number of dogs has something to do with this; but as wild animals and birds become more involved, state departments of conservation have increasing responsibility. And though county programs may be carried out locally, state department of agriculture or livestock sanitary officials have been given a general surveillance and can, in fact, regulate certain aspects of the local program—method of vaccination, deadlines for certifications to be made, and intervals between vaccinations, for example.

Where public health districts or local departments have been organized, the responsibility ordinarily assumed by a municipality or county may be transferred to them. Townships have some health authority—the extent depending on legislative authorization. In Illinois, for example, the assessor, supervisor, and town clerk are a board of health with considerable authority in case they choose to use it: They can quarantine, restrict movement, and require vaccination (unless there is a state law lodging this function with the county).

In empowering local units to engage in animal disease control, the legislature must avoid an undue delegation of authority. Adequate means of determining disease must be provided by law, and there must be uniform and reasonable procedures if owners are to be subjected to quarantine or required to destroy animals.

Though a considerable local authority exists (some of which may be of constitutional origin), the prime mover is the legislature. It has a responsibility for state-wide coordination, for laying down the rules which make local programs effective, for establishing and financing needed research, and for achieving a proper meshing of its efforts with those of the federal government and other states.

The growing importance of wild animals in the whole rabies control program focuses attention on the necessity of involving additional agencies—state departments of conservation for example—and of achieving essential coordination of effort.

Finally, lest undue emphasis be placed on law and regulation, it must be recognized that research, education, understanding, and voluntary cooperation are the real keys to final solution of any serious animal—or human—disease problem.

Discussion--Legal Aspects and Ordinances in Rabies Control

Clarence F. Manziano, D.V.M.[1]

The incidence of rabies in bats and wildlife indicates the importance of rabies control laws which will be practical and effective in preventing rabies in man and eventually eradicating this disease in the United States and the rest of the world.

How can we protect the urban population from rabies, and how can we make a rabies program effective? In the past decade we have seen a marked increase in our pet population and the development of urban communities in areas which were once the sanctuary of wildlife. To some extent the biologic balance has been destroyed, and our methods of disease control and eradication in urban areas must be re-evaluated.

Any Rabies Control Act promulgated for the common good must include the following provisions:

1. Licensing of kennels, pet shops, and pounds.
2. Elimination of the stray-dog population.
3. Licensing and registration of all pet animals.
4. Vaccination of all pet animals susceptible to rabies.
5. Mandatory reporting of all bite cases.
6. Confinement of animals suspected of having attacked or bitten a person.
7. Supervision (where possible) of the rabies control program by veterinarians.

It is important that the Rabies Control Act specifically enables the health authority to promulgate rules and regulations which will have the effect of law in order to cope with an emergency not specifically outlined in the Rabies Control Act.

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ANIMAL BITE WOUNDS AND TREATMENT

S. P. Leinbach, M.D., Chairman

Local Wound Treatment of Animal Bites

Donald J. Dean, D.V.M.[1]

Although the fate of rabies virus within the body is poorly understood, at least in individuals in which the interval between exposure and onset of symptoms is prolonged, evidence is unequivocal that virus customarily moves in animals from site of exposure to the central nervous system via the peripheral nerves. Exceptions in experimental animals include the young, animals of a highly susceptible species, or those in which resistance has been altered by intracerebral trauma or shock. Airborne transmission is occasionally possible (1, 2). Since in most instances virus presumably tends to become fixed in nerve tissue shortly after exposure, prompt (3) adequate local treatment is of paramount importance in preventing disease. Such treatment, supplemented by the use of rabies antiserum and/or vaccine as indicated, must usually be given before the infectivity of the biting animal has been determined by laboratory examination. This paper reviews the principles involved and makes specific recommendations regarding local treatment.

The interval between exposure and onset of symptoms in untreated individuals dying of rabies has remained relatively constant in widely scattered geographic areas and over a long period of time (Table 1) (4). Importantly, the interval between exposure and onset of symptoms is 30 days or less in 14 to 42 percent of such cases. Of the 18 deaths recorded in the United States from 1955 to 1962, the interval between exposure and onset of symptoms in seven persons (38.9 percent) was 14 to 21 days; the median was 35 days with a range of 14 to 120 days. Certainly time intervals of this sort lessen the confidence placed in vaccine alone and emphasize the importance of early, adequate wound treatment and serum therapy.

First-aid procedures are recommended in all rabies exposures, but particularly when a delay is anticipated before competent medical treatment can be obtained. Fortunately many purported exposures to rabies are dubious or consist of bruises, abrasions, lacerations, and other minor wounds. Wounds should be encouraged to bleed freely whenever practical. The effectiveness of simple first-aid procedures in guinea pigs suggests that similar procedures may be effective in man also (Table 2). Marked sparing effect has resulted from the treatment of deep cutaneous wounds three hours after infection with approximately 1,000,000 LD_{50} of fixed rabies virus by

Table 1.—*Interval between exposure and onset of symptoms in untreated persons dying of rabies*

Institute or worker	City or country	Total cases	Incubation period (days): 0 to 30		31 to 60		61 to 90		Over 90	
			Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Comite d'Hygiene, 1862 to 1872..................	France...	170	38	22.4	74	43.5	35	20.6	23	13.5
Nitsch, 1887 to 1905	Cracow ..	72	10	13.9	23	31.9	16	22.2	23	31.9
Busson, (?) to 1929	Vienna ..	35	7	20.0	17	48.6	9	25.7	2	5.7
Högyes, 1886 to 1897.....	Hungary..	210	58	27.6	80	38.1	46	21.9	26	12.3
Babes Institute, 1888 to 1938..................	Bucharest	290	.....	25.2	.....	38.5	.....	18.0	......	17.7
Dodero, 1898 to 1937.....	N.Vietnam	54	21	38.9	26	48.1	7	13.0	......	....
Humphrey, 1955 to 1962...	United States..	18	7	38.9	[1]8	44.4	2	11.1	1	5.6
Pasteur Institute, 1930 to July 1963	Coonoor .	115	48	41.7	45	39.1	13	11.3	9	7.8

[1]Includes one case with possible incubation period of 27 days.

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Table 2.—*Use of first-aid procedures in treating superficial wounds three hours after infection*

[S = difference from controls is statistically significant; HS = highly significant]

Treatment Substance	Experiment[1]				Total	
	1	2	3	4	Number reacting[1]	Percent reacting
Tap water	1/5 (S)	0/5 (HS)	0/4 (S)	0/5	1/19 (HS)	5.3
20% soap	0/5 (HS)	1/4	1/5 (S)	0/5	2/19 (HS)	10.5
Ivory soap	1/5 (S)	1/5 (S)	0/5 (HS)	0/5	2/20 (HS)	10.0
Benzalkonium chloride (1%)	1/5 (S)	0/5 (HS)	1/5 (S)	0/5	2/20 (HS)	10.0
Ivory soap and serum	1/5 (S)	0/5 (HS)	1/5 (S)	0/5	2/20 (HS)	10.0
Controls	5/5	5/5	5/5	3/5	18/20	90.0

[1]Results expressed as the number of animals reacting over the number inoculated.

scrubbing and flushing the wound with cotton pledgets impregnated with warm tap water, 20 percent soap solution, 1 percent aqueous benzalkonium chloride, or Ivory Soap and water, both with and without the addition of topically applied rabies antiserum (5). Despite severe challenge as manifested by 90 percent mortality in the control animals, not more than two animals in each treated group died of rabies; these differences between controls and treated groups are highly significant statistically. Trappers, laboratory workers, and others in high risk occupations should, in addition to being vaccinated prior to exposure, have ready access to first-aid supplies including 1 percent aqueous Zephiran and/or 20 percent soft soap solution. Wherever practical, hyperimmune serum or its gamma globulin preparation should be available for possible topical application.

Treatment by the physician should include thorough cleansing and debridement followed by thorough swabbing and irrigation of the wound with copious amounts of a 1 percent aqueous solution of benzalkonium chloride (Zephiran) or 20 percent soft soap solution. Such treatment has been shown to be effective by many workers (5, 6, 7). However, Zephiran should be used judiciously on or near delicate tissues. Other substances should not be used without adequate prior testing. Quaternary ammonia compounds, for example, are not equally effective in preventing rabies (8). Adequate cleansing with benzalkonium chloride or soap is believed to be at least as effective and probably more so than fuming nitric acid in wounds that permit its application. Immediate suturing of the wound is not generally advised since it may contribute to the development of rabies. Antibiotics presently available do not affect rabies virus but may be helpful in preventing bacterial infection.

Failure to reduce materially the hazard of rabies in animals with deep puncture wounds by swabbing with saline or superficial flushing with serum emphasizes the need for adequate cleaning or debridement and the necessity for using the most effective drugs available. As previously reported (5), groups of guinea pigs with deep puncture wounds infected with 1,000,000 LD_{50} of fixed rabies virus were treated by swabbing with saline or with serum applied topically or injected intramuscularly (Table 3). In sharp contrast to the more or less negative effect of such treatment, impressive results were obtained when hyperimmune antirabies serum was instilled deep into the wound either by deep flushing, a combination of flushing and swabbing with serum-impregnated cotton swabs, or swabbing supplemented with intramuscular injection around the wound.

The effectiveness of topical application of antirabies serum was further explored in groups of guinea pigs with deep puncture wounds similarly infected with CVS virus and treated 3 hours

Table 3.—*Comparative efficacy of different methods of treatment with rabies antiserum in deep puncture wounds in guinea pigs*

[HS = difference from controls is statistically highly significant]

Treatment method[1]	Units of antiserum	Number reacting[2]	Percent reacting
Swab	<41.3	5/20 (HS)	25.0
Swab (opposite leg)	<41.3	17/19	89.5
External flushing	41.3	16/20	80.0
Deep flushing	41.3	1/19 (HS)	5.3
Flushing and swabbing	<82.6	0/18 (HS)	0.0
Swab + intramuscular infiltration	<82.6	1/19 (HS)	5.3
Intramuscular injection (opposite leg)	82.6	12/20	60.0
Controls	....	16/19	84.2

[1]Treatment was given approximately one hour after infection.
[2]Results expressed as the number of animals reacting over the number inoculated.

thereafter with liquid antirabies serum of canine origin or fractions thereof obtained according to the method of Deutsch (9) (See Table 4). Mortality in untreated controls was 8 in 15 (53.3 percent), whereas only 2 of 15 (13.3 percent) whose wounds were flushed with 0.25 ml of liquid antirabies serum succumbed. Mortality in animals treated with globulin 1 (precipitate B) obtained from 2.84 ml of immune serum and globulin 2 (precipitate C) obtained from 11.1 ml of the same serum was 1 in 15 (6.7 percent) and 4 in 10 (40 percent) respectively. All animals treated with similar amounts of globulin 1 powder reconstituted in saline survived. Mortality in animals with uninfected wounds in the opposite leg similarly treated was 6 in 10 (60 percent) indicating that the sparing effect resulted from local rather than systemic action. Excellent results were also obtained in the treatment of superficial wounds with globulin preparations.

Table 4.—*Comparative efficacy of antirabies serum or its globulin fractions in preventing rabies in guinea pigs with deep puncture wounds*

Treatment substance	Serum equivalent per pig	Reactors	
		Number	Percent
Liquid antirabies serum...	0.25 ml.	2/15	13.3
Globulin 1 powder (Precipitate B).........	2.84 ml.	1/15	6.7
Globulin 2 powder (Precipitate C).........	11.1 ml.	4/10	40.0
Reconstituted globulin 1..	2.84 ml.	0/15	0.0
Globulin 1 powder (opposite leg).........	2.84 ml.	6/10	60.0
Controls...............	....	8/15	53.3

Since topical application of antirabies serum is remarkably effective in preventing rabies in experimental animals, similar use should be considered in man whether or not serum is given systemically. When used, very potent serum should be applied thoroughly to all surfaces of the wound after adequate debridement and cleansing. The WHO Expert Committee on Rabies recommends that the topical application of antirabies serum or its liquid or powdered globulin preparations be optionally considered in all exposures and used in all cases involving severe exposure. Recipients should be tested for sensitivity to serum prior to its use.

The WHO Expert Committee on Rabies has long recommended the use of serum infiltrated into the tissue beneath the wound in patients whose exposure justifies parenteral inoculation of serum (9). If used, at least 5 ml should be infiltrated into the tissue surrounding the wound when the site permits. Since untoward side effects may follow the use of serum, it should not be used lightly, and parenteral injection is not presently recommended in exposures where there is little risk of rabies or where local treatment supplemented by vaccine is considered adequate.

The mode of action of the various substances used for local treatment is varied or in some instances unknown. Most solutions tend to flush out or dilute the virus mechanically; some, such as antiserum, benzalkonium chloride, or soap are virucidal, others, possibly including benzalkonium chloride, may also induce nerve block at the site of exposure or otherwise interfere with nerve-borne transmission of virus. In addition to possible destruction of virus, cautery or substances such as fuming nitric acid may destroy or block nerves at the site of exposure.

Nerve-blocking agents have exerted a marked sparing effect in animals when inoculated intramuscularly proximal to the site of infection (5, 7, 8). Although some blocking agents may be virucidal, their greatest effect is probably due to interference with the passage of virus centripetally via peripheral nerves for long enough to allow virus titer to drop below the infectious threshold. Their role in preventing rabies in man requires further evaluation.

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Discussion--The Development of Human Rabies Immune Globulin

William G. Winkler, D.V.M.[1]

SUMMARY

Because of the high reaction rate in individuals receiving hyperimmune horse serum for anti-rabies treatment, it seems desirable to develop a rabies immune globulin of human origin which would have a minimal reaction rate.

Studies at the Communicable Disease Center have revealed that a human rabies immune globulin may be prepared from human serum and that this product can be made as potent as the presently available horse serum. Tests in laboratory animals revealed that the human product will protect at least as well as the horse product. Additional testing is currently under way. The greatest drawback to the commercial production of this type product lies in the fact that it is difficult to obtain adequate quantities of hyper-immune human serum for globulin production.

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Post-exposure Vaccination and Antiserum Prophylaxis of Rabies in Man

Karl Habel, M.D.[1]

The combined use of a single dose of antiserum followed by a course of 21 daily doses of vaccine, plus booster doses, is the most effective method of post-exposure prophylaxis of rabies in man. Future improvements will be aimed at increased purity of vaccine and antiserum to assure safety while retaining high levels of potency.

Although many of us have been and continue to be busy attempting to improve rabies vaccines for use in man, the principles and general methods involved in their production and use are still the same as in the days of Pasteur. However, rabies research has followed the lead of modern developments with other virus agents so that new technics and more quantitative standardized procedures have increased the efficacy of rabies vaccines.

It was recognized very early in the use of vaccine prophylaxis that this measure was not sufficient to prevent rabies in all circumstances, and even later when potency tests assured the use of good vaccines, it was recognized that vaccine alone was relatively ineffective in the face of severe exposures. Thus, an old idea was reinvestigated and the combined use of antiserum and vaccine was found to be the best post-exposure prophylaxis. In fact, the chief advances in the specific prevention of rabies in man since Pasteur have been in the development of more potent and safer vaccines and the establishment of the antiserum-vaccine treatment as the most effective method.

Pertinent Basic Facts. Two facts in the situation of exposure of man to rabies continue to be the basis of specific prophylaxis after exposure. The first is the unique nature of the exposure, where not only the exact time but also the exact site of contact with the virus is known. The second feature is the prolonged incubation period, which provides time for active immunization before the virus has reached and destroyed vital cells. Definitive evidence of the nature of the protective mechanisms involved in effective post-exposure immunization is still lacking. Thus far, there is no evidence that interference or interferon plays a role. Even though an impressive amount of experimental data both in animals and in man has been accumulated concerning circulating antirabies antibodies in relationship to vaccine and antiserum administration, the role of antibody in post-exposure prophylaxis is not clearly defined. At the present time it is felt that serum antibodies play an important part in the effectiveness of post-exposure prophylaxis, but probably do not represent the only mechanism responsible for it.

Although certain biological properties of various strains of rabies virus found in nature or after laboratory manipulation can be shown to differ, there is very little evidence of marked antigenic variation. Virulence for various animal species on inoculation by different routes has been known to vary since the early days of rabies research, and the loss of virulence on adaptation to different species has been the basis for the development of attenuated live virus vaccines. There is evidence that different strains of virus can vary quantitatively in their antigenicity, but in all instances there is substantial crossing between strains when tested by direct challenge of immunized animals or by serum neutralization tests. The lack of a good quantitative technic, such as the plaque method, has been a limiting factor in demonstrating small antigenic differences which probably exist. It is this evidence of relative uniformity of the rabies virus antigen that makes possible the worldwide use of vaccines and antisera prepared against standard virus strains.

Vaccines. With the development of a standardized quantitative potency test in mice, it was found that a number of vaccines in use at that time were low in immunizing potency (8). Vaccine production methods were modified to obtain higher amounts of virus in the vaccine source material, and to inactivate the virus in a way to maximally preserve the antigenicity. As a result, the potency increased to a satisfactory level.

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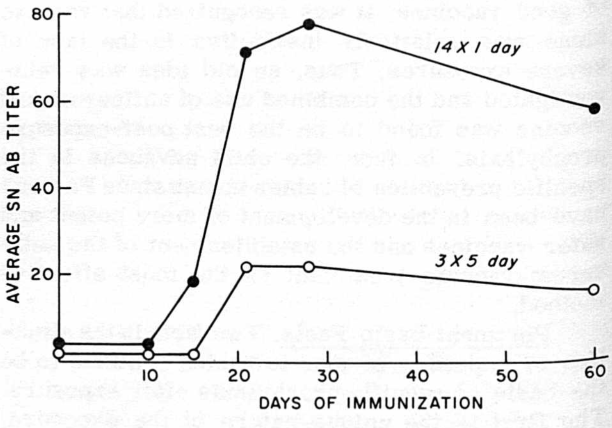
Brain tissue vaccine continues to be the type most widely used throughout the world, with the original or modified Semple and Fermi phenolized products being the most popular. Most of the recent modifications of brain tissue vaccines have involved new methods of inactivation. Thus it has been shown that consistently high-potency vaccines could be prepared by ultraviolet irradiation, merthiolate, 8-propriolactone and even autolytic inactivation of virus. The attitude of the World Health Organization's Expert Committee on Rabies toward development of new rabies vaccines has been that any method is satisfactory if the vaccine can be proven both potent and safe. It is concerning safety that most efforts have been made in recent years to develop a practical vaccine from some virus source other than infected adult mammalian brain tissue in order to reduce or eliminate post-vaccinal complications involving the central nervous system.

Progress has been made in this area, although the ultimate goal of a purified virus vaccine completely free of tissue components has not yet been achieved. The adaptation of rabies virus to growth in the chick embryo (Flury strain), which was so important for improved canine vaccination, offered promise for use in man. However, it was soon found that this attenuated virus showed no evidence of multiplying in man, and that multiple doses were required for antibody response (12). The Flury chick embryo virus has the disadvantage of relatively low virus titers (10^3 to 10^4), and the antigenic mass is too small to make a potent inactivated vaccine; but when multiple doses of the live virus preparations are used,they produce satisfactory antibody levels in man. Higher titering virus yields were obtained by using duck embryos (11) or very young chick embryos (18), and potent inactivated vaccines could thus be prepared. In fact, the commercially available duck embryo vaccine is probably the most frequently, routinely used vaccine in the United States today. The potency of the inactivated virus duck embryo vaccine is consistently lower than good brain tissue vaccines, although still at a satisfactory level (4). There was experimental evidence suggesting that vaccines made from infected avian embryos would be free of the factor causing vaccine paralysis in man, and the experience with the duck embryo vaccine indicates a great reduction in this hazard (7). However, such a reaction apparently can occur at a much reduced incidence.

The use of brains of young animals which are free of the paralytic factor was proposed, and inactivated vaccines made from the brains of infected suckling mice (6), as well as newborn rats (15), are now in use. The establishment of a tissue culture source of virus for vaccine production appears to be the most promising possibility at this time (5, 16). The chief factors keeping this from being accomplished are: (1) virus yields in most tissue culture systems are too low for making a potent inactivated virus vaccine (under 10^5), (2) the cells used in a tissue culture vaccine must be acceptable to public health authorities (normal untransformed cells free of extraneous infectious agents) and readily available in large quantitites, and (3) the tissue culture medium should be free of any possible sensitizing foreign antigens, such as heterologous serum. Some of these goals appear within reach in view of recent developments in the cultivation of rabies in tissue culture systems.

Although reduced schedules with fewer doses of vaccine are effective in animal experiments involving pre-exposure immunization (10), serum antibody responses in humans are most rapid and achieve higher levels with the standard multiple daily dose regimen (Fig. 1). The volume and concentration of the vaccine as well as the number of daily doses recommended varies throughout the world, but, in general, the equivalent of 2 ml of a 5 percent tissue suspension should be given daily for 14 days. Even where vaccine alone is used as well as when combined with antiserum, it is strongly recommended that booster doses of vaccine (preferably non-nervous tissue type) be given at 10 and 20 or more days after the last daily dose (see below).

Figure 1.–*Serum antibody response (average titer–10 individuals per group) with 14 daily doses vs. 3 doses, 5 days apart of 2.0 ml. of 5% phenolized brain tissue vaccine(2)*



The importance of the potency of the vaccine has been pointed out many times in the past but needs re-emphasizing. No one can assume that his method of vaccine production assures accepted levels of potency. Every production batch of vaccine must be checked in mice and be proven potent. It must also be remembered that the vaccine must be potent not only at the time of production but at the time of use. This means that all production laboratories should investigate the stability of their vaccine's potency under a variety of environmental conditions before establishing the effective dating period. All types of vaccines, including phenolized products, can now be dried (14), and this when done properly with the use of stabilizers should increase potency stability.

Antiserum in Prophylaxis. Although the use of antirabies serum in post-exposure prophylaxis goes back many years, its undoubted efficacy has been established only in the last 13 years through the studies of the WHO Expert Committee on Rabies. The superior results obtained experimentally (9) were confirmed in a field trial in Iran in 1953 (3). Similar excellent results have since been obtained in the U.S.S.R. (13) and other countries. Many experimental studies in humans (Fig. 2) have established that the combined use of a single dose of antiserum given at the start of treatment, and a course of at least 14 daily doses of vaccine is the best specific prophylaxis available today. However, it has been found that the antibody present in the antiserum tends to inhibit the antigenic effect of the vaccine (Fig. 3). To overcome this, it is now recommended that booster doses of vaccine be given after completion of the usual daily dose schedule. Originally, booster doses at 10 and 20 days after the last regular dose were recommended, but in view of experience with booster effects of other antigens, a more effective regimen might be boosters at 20 days, 2 months, and 6 months.

There has been some speculation concerning the number of daily doses of vaccine to be used in conjunction with antiserum unrelated to the booster doses to be used in all instances. Although 14 daily doses are considered adequate, the best results thus far obtained in Iran and Russia have utilized at least 21 daily vaccine doses. In the past it has been felt adequate to use a course of vaccine, including booster doses, without antiserum for mild exposures, but in view of accumulating experience with the outstanding efficacy of combined antiserum and vaccine this is now recommended in all types of exposure. The booster doses, where possible, should be of non-nervous tissue vaccine. Care must be taken in the use of antiserum to prevent anaphylactic reactions (skin test), and serum sickness is not an unusual complication. The possibility of antirabies serum produced in humans is now being investigated. As in the case of vaccines, the importance of using serum of proven potency cannot be over-emphasized.

Indications for Specific Prophylaxis. There have been no major changes in the indications for specific prophylaxis except that all bites by rabid wild animals are considered "severe" exposures no matter what the nature of the bite, and all bites by bats are treated no matter what

Figure 2.–*Continuing serum antibody levels with antiserum (0.5 ml. per kg. body weight) and 12 daily doses of phenolized vaccine (0.5 ml. of 20% brain tissue). Average serum antibody titers of 10 individuals per group (1)*

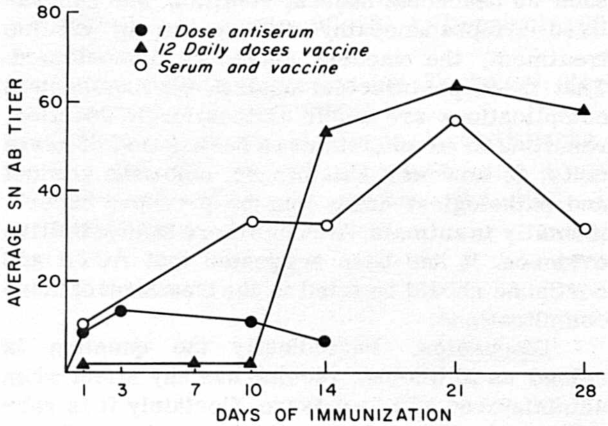
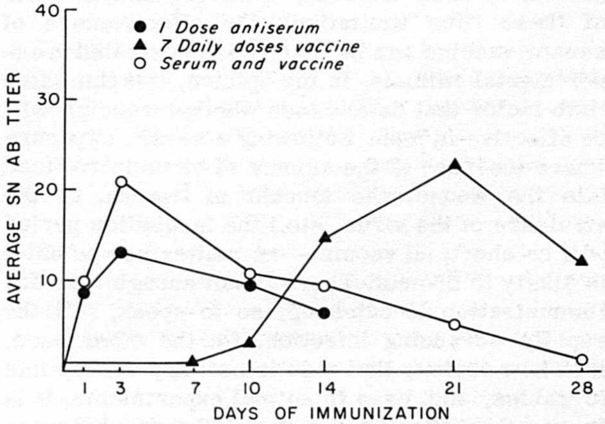


Figure 3.–*Interference by antiserum (0.5 ml. per kg. body weight) of the antibody response to 7 daily doses of phenolized brain tissue vaccine (0.5 ml. of 20% tissue). Average serum antibody titers of 10 individuals per group (1)*



the clinical condition of the biting animal. Contamination of the sound skin by saliva from a rabid animal is not considered an exposure and is not treated. The details of the latest WHO recommendations in these matters are given in the fifth report of the WHO Expert Committee on Rabies (17).

Reactions to Vaccine. Reactions to vaccine are still of clinical importance. When reactions are based on sensitivity to the species specific protein from the animal in which the vaccine was produced, the problem can usually be overcome by changing to a vaccine made from a different species (vaccine for canine use is usually available and made from another animal species). Neurological involvement is still a complication of antirabies vaccine treatment, especially where nervous tissue vaccine is used, and probably will not be completely eliminated until purified virus vaccines are available, or non-nervous tissue cultures can be used in production. These neurological complications usually occur after completion of the vaccine course, and when evidence such as headache, nausea, vomiting, and generalized lymphadenopathy develop during vaccine treatment, the vaccine should be discontinued. That these postvaccinal central nervous system complications are due to an isoallergic reaction, resulting in an auto-immune destruction of nerve cells, is now well established, since the clinical and pathological entity can be produced experimentally in animals. Although there is no definitive evidence, it has been suggested that ACTH and cortisone should be tried in the treatment of these complications.

Discussion. Periodically the question is raised as to whether vaccine has any effect when administered after exposure. Certainly it is very difficult to obtain any positive experimental evidence, but this is probably due to the time factor. To produce rabies in the majority of control animals, one must use a large inoculum of virus, which usually results in a short incubation period. It is of interest, however, that in spite of these time limitations the effectiveness of serum-vaccine can be readily demonstrated in experimental animals. In my opinion, it is this same time factor that determines whether vaccine will be effective in man. Following a severe exposure where (because of the amount of virus introduced into the wound, the amount of trauma, or the virulence of the virus, etc.) the incubation period will be short, no vaccine—no matter how potent—is likely to protect. There is not enough time for immunization to catch up, so to speak, with the rapidly advancing infection. On the other hand, it is now obvious that man is not very susceptible to rabies, and, even in animal experiments, it is frequently difficult to produce 100 percent disease after intramuscular challenge with street virus. Therefore, in the case of very mild exposures in man, many would survive without vaccine treatment. However, there is no doubt that an intermediate level of exposure exists in which the incubation period would be prolonged, and here vaccine can make the difference between survival and death.

The time factor also appears to explain the efficacy of the serum-vaccine prophylaxis. In post-exposure treatment of experimental animals when antiserum alone is given, there is frequently no reduction in mortality but a marked prolongation of the incubation period. This, of course, is precisely what is needed for the vaccine to be effective. Active antibody produced by the vaccine appears before the passive antibody from the serum disappears, thus providing circulating antibody continuously from the first day of treatment. The demonstration of interference with the antigenicity of the vaccine by the antibody from the dose of serum has somewhat complicated the serum-vaccine treatment. To overcome this interference a single dose of antiserum and 21 daily doses of vaccine, plus booster doses, is now recommended. There is good reason to except that this regimen will produce the high efficiency of the serum-vaccine treatment while eliminating the interference effect.

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Discussion--Post-exposure Vaccination and Antiserum Prophylaxis of Rabies in Man

F. Bruce Peck, Jr., M.D.[1]

The post-exposure rabies prophylaxis discussion presented by Dr. Habel leaves little for me to add, especially from the point of view of current recommendations for the use of various treatment regimens. I do feel, however, that certain points deserve re-emphasis.

It should be remembered that the Expert Committee Recommendations must be designed to meet any situation that develops in any area in the world, not just for one particular locality. The committee has, in my opinion, done an excellent job in keeping their recommendations up to date. The important thing to keep in mind, however, is that the recommendations must be augmented with information on the local rabies situation. The treatment of dog bites in areas where rabies does not exist will certainly be different from treatment of the same bite in a locality where canine and/or wild animal rabies is prevalent.

From time to time there have been questions as to why a standardized regimen could not be set up so that all physicians could follow the same treatment plan. The answer is obvious—the treatment of the patient is based not only on WHO recommendations, but must also take into account the local rabies situation. What we must all strive for is the efficient evaluation of many variables so that the physician can make an adequate judgment. This can only be done through well informed public health groups and adequate basic education of physicians in the principles of rabies prophylaxis.

Public health departments must be able at any time to assess the local rabies situation and advise physicians accordingly. Physicians must have an understanding of the problems and risks that are involved. This means good basic medical school education, as well as an up-to-date knowledge of the current situation. All too often we are called by physicians faced with a treatment decision, and they state they had no formal lectures in school on rabies immunization procedures. This is one area in which improvement is needed.

I have one additional comment to make regarding post-exposure treatment. As you are now well aware, there is a tremendous amount of work in progress in the further development and refinement of rabies vaccines and antisera. Studies on the production and use of human antirabies serum are underway and hopefully will ultimately result in a preparation which will replace equine antiserum, and thus do away with the everpresent hazard of serum sickness or other allergic reactions to equine protein.

Historically, rabies vaccines have been extremely crude tissue suspensions of the central nervous system. The development of avian vaccine, such as duck embryo, has virtually eliminated specific neurological reactions associated with post-exposure treatment. However, it still consists of crude suspensions of embryo protein, and even though embryo protein is poorly antigenic, local and nonspecific systemic reactions are still a problem. The efforts toward producing refined vaccines such as those made in tissue culture, or purified antigens made from mouse brain or other tissue, are good indications that future vaccines are currently being developed. Without question, there will be greatly improved vaccines in the not-too-distant future. The state of the art of producing biological antigens has advanced at a rapid pace during the past decade, and we can now predict with confidence that future rabies vaccines will have a high degree of purity, clinical safety, and antigenicity.

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Pre-exposure Rabies Vaccination

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The development of avian origin rabies vaccines stimulated investigations using such vaccines as pre-exposure immunizing agents (1-5). These avian products are considered safer than the nervous tissue vaccines, since embryonic tissues are poorly antigenic (6). Until rabies vaccines of chick and duck embryo origin were developed, the danger of isoallergic encephalomyelitis caused by nervous tissue vaccine precluded any definitive studies on the feasibility of immunizing man prior to exposure.

The present investigations were undertaken to determine the most satisfactory, practical regimen for pre-exposure rabies immunization in humans. The two vaccines used were the duck and chicken embryo antirabies vaccines (DEV and CEV). DEV is a killed product, commercially available as a human antirabies vaccine for therapeutic use. CEV is a highly modified live virus product and was available for experimental use only. The development of these vaccines has been previously reported (7-9).

Method of Study. A total of 540 volunteers from four veterinary schools in the United States were given the rabies vaccines in various regimens. The first study was designed to compare the effectiveness of DEV with CEV when given intradermally. Volunteers from two schools, A and B, were divided into two approximately equal groups. One group from each school received only the DEV, the other received only the CEV. The same lot numbers of vaccines were used in the volunteers of both schools. The regimen of vaccination consisted of a primary series of three injections given on days 1, 8, and 15, plus a booster on day 56. All inoculations consisted of 0.2 ml of vaccine administered intradermally in the lateral aspect of the upper arm (deltoid region).

The second study at schools C and D was designed to compare the effectiveness of DEV when given (a) intradermally or subcutaneously, and (b) at different time intervals. A total of four inoculations were used in each regimen, three in the primary series and one booster.

In the third study, students at school C were divided into two groups, the first was given a primary subcutaneous series of two inoculations of DEV and the second was given three inoculations. Both groups were given one booster.

A blood sample was collected from each volunteer 1 month after the final injection was given. The serum was removed from each specimen and was sent to the Rabies Laboratory of the Communicable Disease Center, where antibody titers were determined. Serum neutralization tests, as prescribed by the World Health Organization (10, 11), were used for determining the titers.

Results. The results are given in terms of the numbers and percent of volunteers showing a positive serum antibody response. Serum samples were considered positive if they protected 50 percent of the mice at a dilution of 1:2 or greater against 10 to 100 mouse LD_{50} of fixed rabies virus.

A summary of the results of the first study in which a series of three inoculations followed by a booster on day 56 is given in Table 1. In school A, 36 percent of the volunteers who received CEV developed titers as compared with 48 percent of those receiving DEV. In school B, 50 percent of those who received CEV and 80 percent of those receiving DEV had positive titers. Thus, the DEV in the school B volunteers elicited a greater proportion of positive responders than the CEV. This difference was shown to be statistically significant (P= .002); whereas the difference between the two vaccine groups in school A was not (P= 0.61).

In the second study at school C (Table 2), the best response occurred in those who received 1.0 ml of vaccine subcutaneously monthly; however, there was no statistically significant difference in the response of the groups.

In school D, 100 percent of those volunteers receiving the vaccine intradermally and 95 percent in those receiving it subcutaneously (Table 3)

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Table 1.—*Individuals showing positive serum antibody titers one month following completion of four inoculations of duck or chicken embryo rabies vaccines*

Vaccine[1]	School A: Number responding[2] / Number vaccinated	School A: Percent responding	School B: Number responding[2] / Number vaccinated	School B: Percent responding
Chicken embryo vaccine	15/42	36	28/56	50
Duck embryo vaccine	20/42	48	49/61	80

[1]0.2 ml of the vaccine administered intradermally at 3 weekly intervals, followed by a booster of the same dose 6 weeks after the third dose.
[2]Positive response indicates serum titer of 1:2 or greater against 10 to 100 mouse LD_{50} of fixed rabies virus.

Table 2.—*Positive SN antibody response to duck embryo rabies vaccine in School C students*

Dose, route and interval[1]	Number responding[2] / Number vaccinated	Percent responding
0.2 ml Intradermal: Weekly . . . 3 plus 1 . .	37/48	77
0.2 ml Intradermal: Monthly . . 3 plus 1 . .	43/53	81
1.0 ml Subcutaneous: Weekly . . . 3 plus 1 . .	42/49	86
1.0 Subcutaneous: Monthly . . 3 plus 1	48/51	94

[1]Indicates interval between the 3 primary inoculations. All 4 groups received a booster 10 months after onset of primary series.
[2]Positive response indicates serum titer of 1:2 or greater against 10 to 100 mouse LD_{50} of fixed rabies virus.

Table 3.—*Positive SN antibody response to duck embryo rabies vaccine in School D students*

Dose, route and interval[1]	Number responding[2] / Number vaccinated	Percent responding
0.2 ml Intradermal: 3 plus 1.	54/54	100
1.0 ml Subcutaneous: 3 plus 1.	54/57	95

[1]Both groups received a primary series of 3 weekly inoculations followed by a booster 10 months later.
[2]Positive response indicates serum titer of 1:2 or greater against 10 to 100 mouse LD_{50} of fixed rabies virus.

Table 4.—*Positive SN antibody response to duck embryo rabies vaccine in School C students*

Dose, route and interval[1]	Number responding[1] / Number vaccinated	Percent responding
1.0 ml Subcutaneous: 2 plus 1.	57/63	90
1.0 ml Subcutaneous: 3 plus 1.	56/62	90

[1]The group receiving two injections a month apart in the primary series received a booster seven months after the second injection. The group receiving three injections a month apart in the primary series received a booster six months after the third injection.
[2]Positive response indicates serum titer of 1:2 or greater against 10 to 100 mouse LD_{50} of fixed rabies virus.

developed detectable antibody. No statistically significant difference was observed between the two groups at school D.

Results of the third study are presented in Table 4. At school C, no difference was noted between the groups receiving three doses of vaccine and the group receiving four doses. In both instances, 90 percent of the volunteers developed a positive rabies antibody titer.

Discussion. An assessment was made of four variables—vaccine, dose, route, and time interval between doses—to determine the most satisfactory regimen for pre-exposure rabies immunization. The DEV was superior to CEV using the same regimen. However, only small differences were noted when DEV was given in varying doses and routes (0.2 ml or 1.0 ml, intradermally or subcutaneously) at different time intervals (weekly or monthly in the primary series).

A consistently higher percentage of volunteers developed detectable antibodies following the subcutaneous inoculations with DEV. The response was less consistent when the DEV was administered intradermally. The difficulty in administering the vaccine intradermally probably accounted for this variation.

On the basis of this study, the following regimen appears to be most practical for pre-exposure rabies immunization: Two subcutaneous inoculations of the DEV a month apart plus a booster 7 months after the second inoculation. One ml of the vaccine should be given in each inoculation, administered in the lateral aspect of the upper arm (deltoid region).

It is recommended that certain high risk segments of the population be given prophylactic rabies immunization. Several schools of veterinary medicine in the United States are already actively engaged in an annual program to immunize veterinary students. Likewise, a few state veterinary associations also recommended that veterinary practitioners receive this protection. Other groups that should receive this vaccine prophylactically include laboratory and wildlife workers as well as people traveling to countries where rabies is a serious epizootic problem. The Armed Forces and Peace Corps have given this vaccine to several thousand personnel going overseas.

A factor to take into consideration is the occurrence of local and systemic reactions to pre-exposure immunization. Local reactions have been reported to occur in approximately 25 percent of the individuals immunized during pre-exposure immunization programs (12). These reactions occur at the injection site and consist of pain and tenderness usually lasting approximately 48 hours. Occasionally, a considerable amount of induration has occurred accompanied by regional lymphadenopathy. These reactions have not been incapacitating. No sterile abscesses or granulomas have been seen. A few cases of malaise and transitory low grade febrile reactions have accompanied the local inflammatory response. These have not been severe.

Although the titer of rabies SN antibody often declines to a low or undetectable level after 6 to 12 months, on the basis of several hundred sera tested, we have found that a booster inoculation resulted in a titer as high as or higher than previously observed. For that reason, a booster every 2 to 3 years is recommended. In persons who have had a pre-exposure rabies prophylaxis series, the use of the full 14-dose immunization schedule following an exposure must still be decided on the individual merits of the particular case in question.

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Discussion--Pre-exposure Rabies Vaccination Experience within the Peace Corps

James E. Banta, M.D. [1]
Jay M. Pomerantz, M.D. [2]

In 44 countries around the globe, there are presently dispersed some 13,000 Peace Corps Volunteers. These Volunteers are widely distributed in both urban and rural situations and are often at considerable distance from medical facilities. They live in close proximity to their host country national counterparts and some in close contact with the local animal population. As a result of this mode of existence, they are presented with a significant hazard from rabies. With few exceptions, rabies is endemic in all of the host countries where Volunteers are stationed. For example, in Lima, Peru, over the past 4-1/2 years, some 47,000 dog bites have been reported (1). And indeed, during the first 9 months of 1964, 493 rabid dogs were isolated. In Thailand, there are 200 to 230 deaths per year, with 20 deaths occurring in Bangkok (2). In the Philippines, there are 270 deaths per year reported—certainly a potentially dangerous hazard (3).

In a recent epidemiologic study reported by Parrish and associates, it was noted that in the United States some 362 dog bites occur per 100,000 population per year (4). This undoubtedly represents under-reporting. It is interesting to note that 76 percent of the individuals bitten were under 20 years of age. By way of comparison amongst Peace Corps Volunteers, there are 3,120 bites per 100,000 per year, and 98 percent occur in individuals 20 years of age and older. It is apparent that the Volunteer's potential rabies exposure rate from dog bites approaches 10 times the United States rate; and the bites occur in an animal population that is by and large uncontrolled.

All Peace Corps Volunteers are given 30 hours of personal health training prior to going overseas; however, the Peace Corps Volunteer does not always fully appreciate particular risks to his health. Hence, not recognizing the danger of rabies, he might neglect to report a potential exposure from an animal bite until a week or more after the exposure has occurred. It can be readily appreciated that this can create considerable anxiety amongst the members of the medical staff responsible for his safety and well being. The work of Fox (5, 6), Peck (7), Tierkel et al. (8), has demonstrated the feasibility of pre-exposure immuno-prophylaxis against rabies. We certainly feel that in the Peace Corps we have a high risk group. Hence, such a program seems to be entirely justified and is feasible.

The program was instituted utilizing duck embryo vaccine (9) given in a series of three inoculations: One cc of vaccine was given at time 0, the second inoculation was given 3 weeks later, and finally, the third inoculation was administered 3 to 6 months later. Approximately 5,000 individuals have been immunized by this regimen.

An important aspect in evaluating any immunization procedure is to determine the magnitude of untoward reactions to the vaccine. These data were solicited from the Peace Corps Medical Consultants at the training sites where the Volunteers are prepared for overseas service, both medically and in terms of their training. Data on 3,427 individuals were received. In this population of 3,427, there were 23 reactions to the immunization procedure as shown in Table 1. Nineteen of the reactions occurred following the first inoculation, while four reactions occurred following the second inoculation. The intensity of the reaction ranged from local edema and induration to generalized anaphylaxis. Actually, only one case of anaphylaxis occurred in this group. The typical reaction was an urticarial response, though there were also many who responded with nausea and/or vomiting, and also abdominal cramps. In all cases, the individuals responded promptly to conservative treatment with antihistamine and occasionally adrenalin. Only in the one case of anaphylaxis was hospitalization necessary, and the Volunteer responded readily to adrenalin and steroid therapy. The reaction followed the first inoculation.

It would seem that a reaction rate of 6 or 7 per 1,000 individuals immunized is not an undue risk in light of the benfit the program provides. The Volunteers, because of the wide dispersion

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Table 1

Patient	Urticaria	Abdominal cramps	Nausea, vomiting	Edema, induration	General rash	Anaphylaxis	Bronchospasm	Unspecified	Inoculum number
1				+					1
2							+		1
3								+	1
4	+								1
5	+		+						1
6			+						1
7				+					2
8	+	+	+						1
9		+					+		1
10	+								1
11	+		+						1
12	+								1
13		+							1
14			+	+					1
15	+								2
16					+				2
17				+					2
18	+		+						1
19		+							1
20	+		+						1
21						+			1
22	+								1
23	+								1
Totals	11	4	7	4	1	1	2	1	

and the logistic problems involved, are not routinely checked for a positive response to vaccination. Rather, at the time of potential exposure to rabies, the individual is given the standard full course of prophylactic immunizations with duck embryo vaccine. It would seem that the rapid anamnesis and the higher titer give significant added protection, particularly in those individuals who fail to report the potential exposure until a week or more after the event has occurred. It also generally obviates the necessity for using antiserum and its attendant hazard of sensitization and serum sickness.

In one study in the Philippines on antibody response following immunization, 20 Volunteers were bled 1 month after the last inoculation, and of this group, 18 of 20 demonstrated significant neutralizing antibody titers—with a response of

Table 2.—*Antibody response to rabies immunization following 3 inocula*[1]

Patient	Titer	Response	Patient	Titer	Response
S.I. ...	1:20	Positive	P.H. ...	1:32	Positive
M.Z. ..	1:50	Positive	R.H. ...	1:50	Positive
R.B. ..	1:50	Positive	M.P. ...	1:32	Positive
J.W. ...	1:20	Positive	M.M. ...	1:50	Positive
F.D. ..	1:50	Positive	C.G. ...	1:50	Positive
R.A. ..	1:50	Positive	J.H. ...	1:50	Positive
M.G. ..	1:12	Borderline	M.G. ...	1:50	Positive
R.H. ..	1:50	Positive	E.M. ...	1:50	Positive
D.C. ..	1:50	Positive	D.L. ...	1:32	Positive
W.S. ..	1:50	Positive	V.C. ...	1:5	Negative

[1]Neutralization technique carried out with sera tested against 15 MLD_{50} Rabies virus by the Rabies Laboratory of the National Communicable Disease Center, USPHS, Atlanta, Georgia.

1:20 or greater to 15 MLD_{50}, as shown in Table 2.

It appears that the present experience, borne of necessity, demonstrates the feasibility of the widespread use of duck embryo vaccine for pre-exposure immuno-prophylaxis against rabies. As other rabies vaccines with an even lower reaction rate are introduced, it would seem entirely feasible for large population groups to be immunized prior to exposure. This could provide significant protection to particular developing countries which have high mortality rates from rabies.

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Discussion--Pre-exposure Rabies Vaccination

John P. Fox, M.D.[1]

As a longtime advocate of pre-exposure immunization against rabies, I applaud the definition of a satisfactory regimen using an available vaccine. Further, I think the principles of the regimen suggested will remain applicable even when still better and safer vaccines are produced.

I would like to take this opportunity to reinforce the evidence presented by Dr. Sikes and also to draw attention to additional factors relevant to sero-response by recalling to your minds some already published data from my own experience.

The regimen described consists basically of a two-dose primary course plus a delayed booster dose. The data presented suggest that the spacing of inocula is very important. This we also found true with HEP chick embryo vaccine with a two-dose course, (1) as shown in the following tabulation:

Interval (days)	No. persons inoculated	Percent Responding
3	14	43
10-20	18	55
30	6	100

Dr. Sikes also found that delay of the booster from 6 weeks to 7 or 10 months was helpful. This conforms with our previous experience also, in that booster effects could be best detected after an interval of 5 or more months.

The level of neutralizing antibody response to the primary course also is related to the response elicited by the booster inoculum (1) as shown in the tabulation below:

Maximum antibody titer after primary course	Number of persons with maximum titer after booster		
	<4	4-31	32+
8+		1	9
4-7	1	1	4
<4	7	1	2

Salk (2) has presented similar data for response to killed polio vaccine. This emphasizes the importance of securing maximum response to the primary course, not only by optimum spacing of inocula but also by using potent vaccine. In this connection, it was found that using comparable immunizing regimens, CNS tissue vaccines (Semple or Harris types) were markedly superior to avian embryo (chick or duck) vaccines as measured by level of antibody response (1).

I also would remind you that post-exposure Pasteur treatment not infrequently serves as pre-exposure immunization which, in the event of another exposure, usually can be recalled quickly with a booster inoculum. Data from 136 persons indicated that when the interval between treatment and booster did not exceed 20 years, failures to respond were chiefly in recently treated persons whose pre-booster antibody titers were already too high to be boosted (1).

Antibody persistence probably will be explored by Dr. Sikes in the future. However, I do have some relevant data. With HEP Flury vaccine, persistence over a 2-year period after a booster was very good in persons whose maximum neutralizing titer after the booster was 1:32 or higher. After a single course of Pasteur treatment, 75 percent possessed antibody for up to 5 years, and when two or more courses had been given, antibody was present uniformly for up to 5 years after the last course and persisted in 90 percent for up to 15 years. While these persons had unusually strenuous primary and booster courses, post-booster antibody may well persist for a long time.

Antibody persistence, however, is less important than persistence of ability to respond to a recall inoculation. While the evidence I have presented related to prior Pasteur treatment and evidence related to tetanus suggest that this may be very long, more data relating to a reasonable pre-exposure regimen would be highly desirable—and, hopefully, also may be obtained in time by Dr. Sikes.

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SYLVATIC RABIES IN THE UNITED STATES

Aaron Christensen, M.D., Chairman

Sylvatic Rabies as a Recreational Problem

James Asa Shield, M.D.[1]

It has been both informative and a pleasure to have been privileged to meet with you yesterday and today. As a psychiatrist and a fox hunter I have a keen interest professionally and personally in this National Rabies Symposium. Those of us who enjoy fox hunting and live in fox hunting country for many reasons are the people most affected by rabies.

One of the great recreational sports is fox hunting. Let me say, right at the start, when we say fox hunting, we don't necessarily mean that sport with horses and hounds. To many sportsmen, fox hunting is night or day hunting with hounds, from a hill top or an automobile. Contrary to the belief that fox hunting is a sport enjoyed only by elegant gentlemen and ladies in pink coats astride their expensive steeds, night fox hunting is a sport pursued all over the land by men of all means. There's the story of the young man who visited his girl every Wednesday night for 10 years, and when a friend asked him why de didn't marry the girl, he said, "Well, it's like this. She says I'm too poor to keep four hounds and a wife but she will marry me if I will give up two hounds. I ain't never bin able to decide which two hounds to give up."

The spell of fox hunting, the dedication of those who follow hounds, the sacrifices they make, the discomforts they endure, have long been a matter of wonder, even to other horsemen and other fox hunters. To a psychiatrist, however, it is no wonder, for fox hunting re-awakens in us a primitive passion for the chase of wild game with running hounds, a passion which is as old as the human race. All sorts and conditions of men, from princes to peasants, have, since time immemorial, been imbued with the lure of the chase, which was originally a struggle for existence.

Deposits found with skeletal remains of Paleolithic man show that animals were hunted 125,000 years ago. Nimrod, the mighty hunter before the Lord in the Book of Genesis, has become almost the generic name for huntsmen. Hunting myths abound from the Golden Age of Greece. Hunting themes are common in Egyptian art. William the Conqueror, who lived in the 11th century, has been called the father of modern hunting. His hounds and horses appear in the beautiful and definitive Bayeux Tapestry. William protected the sport of the hunt with rather more stringent measures than we are considering today. He ordered that anyone who killed a dog should have his eyes put out.

There would be no fox hunting without hounds, and foxhound packs have existed in America since Colonial days. The history of the white man's coming to America and the importation of hounds run hand in hand. The Complete Dog Book of the American Kennel Club has this to say about the American Foxhound: "According to well-known authorities on the American hound, the first mention that we have of hound importations to America appears in a diary of one of DeSoto's retainers. It is further mentioned that these hounds were utilized to hunt Indians instead of foxes and hare.

"From this same good authority we learn that in 1650, Robert Brooke sailed for the Crown Colony in America, taking his pack of hounds with him, which were the taproot of several strains of American hounds and remained in the family for nearly 300 years. Then Mr. Thomas Walker of Albemarle County, Virginia, imported hounds from England in 1742; in 1770 George Washington subscribed to the importation of hounds from England, and in 1786 received some French hounds from Lafayette, their voices being 'like the bells of Moscow.'"

George Washington's diary contains scarcely a page dwelling on his domestic life that doesn't mention fox hunting. His diary contains at least 200 references to individual hunts, including whether the fox was caught, the weather, and the scenting conditions.

This great sport of fox hunting is dependent on a normal, healthy fox population, and a normal fox population is dependent on a normal balance of wildlife in its natural habitat. At the same time the fox hunter keeps the fox from Farmer Brown's chicken house, he leaves enough foxes to keep the destructive field mouse population in control.

A disease that makes the farmer individually, and/or collectively, want to exterminate the fox by killing all healthy as well as diseased foxes, or

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any species of wild animals, is bad. The price of eliminating certain wild animals in an area can be dangerous and a deterrent to the survival of other wild animals, and to the economic welfare of the people of the land.

Rabies makes the fox entirely unwanted by the farmer. An outbreak of rabies among local foxes in any community is followed by reasonable, and at times hysterical, demands that the fox be trapped and be eliminated. This course would end fox hunting.

However, we appreciate the farmer's fear when a rabid fox is reported in the neighborhood. We are concerned about the child that may be bitten. We are unhappy about the loss of a valuable cow or horse. It is not important that there are very few instances of rabies causing loss of domestic animals, and that percentage-wise there are very, very few humans bitten by rabid animals. A few are too many.

Fox hunters are well aware that rabies is a rightly feared disease. We are anxious to eliminate rabies. As we know, any rabid animal, dog, fox, or skunk, is a potential infector before the disease develops to the paralytic terminal stage and kills its host. Fox hunters in Virginia have taken out their packs of rabies-immune-by-vaccination hounds to find and to kill rabid foxes. We are equally aggressive in our support of a research program which has as its purpose a method of eradicating rabies in wild and domestic animals, and in man.

American fox hunters, in keeping their thousands of hounds, kennels, stables, and miles of hunting country, pour millions of dollars in the farmers' pockets and into the tax collectors' bags—county, state and federal.

In the United States and Canada, there are 115 organized hunts formally recognized by the National Association of Masters of Foxhounds. The cost of maintaining a recognized hunt varies from a few thousand dollars to many thousands. The hunt membership individually has thousands in horses, millions in land ownership, thousands in daily payrolls. Thus, recognized hunts bring new wealth to any hunt country. More important, they bring to the community men and women who become useful citizens who give of themselves, their talents, and their money.

In Virginia alone, there are more than 200,000 licensed hounds. It is estimated that these 200,000 hounds eat $4,000,000 worth of food per year. Where there are organized packs of foxhounds or organized groups of fox hunters, it naturally follows that there will be field trials and bench shows. The Culpeper, Virginia, Chamber of Commerce estimated that just one such 4-day meet in 1965 netted the community over $150,000 in services rendered to individuals who showed their hounds.

Some fox hunting requires horses as well as hounds. Horses were brought to Jamestown by the English settlers. A little known fact is that originally American Indians had no horses, they had to depend on Spanish imports through Mexico and Florida for picturesque "old paint." Horses were important enough to the early settlers to preempt space on the little ships from England, and they remain an important economic factor today.

Fox hunting sparked the interest of many men who are in the horse business. Virginia's horse industry, for which I have some figures, should give us an idea of the economic impact made by this industry.

There are presently about 75,000 horses and ponies in use in Virginia, and of this number 11,500 are thoroughbreds. Last year thoroughbred sales in Virginia involved more than 4-1/2 million dollars. In a recent survey, expenses on thoroughbred farms and racing stables in Virginia amounted to $9,400,000, not including taxes. Available figures place the total number of people involved in the Virginia horse industry at well above 10,000. These figures could be repeated many times over for other areas of the United States. Kentucky immediately comes to mind with the running of the Derby tomorrow. The great Maryland Hunt Cup was run last weekend, certainly the greatest steeplechase in America. In short, there would be no formal fox hunting without horses. And there would be a lot less money in horses without fox hunting.

Fox hunting is a community asset. In addition to furnishing sport for local residents, it attracts new residents who are valuable neighborhood additions. It raises the value of land throughout the whole hunting country. This increased value, plus the improvements made by fox hunters to soil fertility, fencing, roads, and buildings, plus increased inventories of livestock, farm machinery, and household possessions, means larger revenues from taxes. Fox hunters spend most of the money for these improvements and added inventories locally. Non-resident fox hunters, who come for the season, rent housing and stabling, provide additional employment, and buy hay, grain, and straw for their horses. Even the transient fox hunter, besides paying capping fees to the hunt, rents hunters and patronizes local hotel, motels, and restaurants.

As an example of what fox hunting can mean to a community, we can look at my home county in Virginia. The Deep Run Hunt was formerly located at the edge of Richmond. About 20 years ago we moved to a nearby county where members, me among them, have bought thousands of acres of land. The entire county has profited from increased taxes made possible by the rapid rise in land value (only in the interest of fox hunting would I endorse skyrocketing assessments).

In summary, in Virginia we have approximately 20,000 resident fox hunters that we know about. Some of those night hunters probably aren't counted because as another story goes, some night hunters become so absorbed in fox chasing that they take their person from the hearth for longer periods than are, perhaps, conducive to good husbandry. There was one who went to a hunt in Kentucky and stopped at a hotel that had a bathroom on both floors and served the soup before the meat and was, therefore, luxurious. He was asked how he could carry on this way, living like a king, with his poor wife and children left alone in that cabin. He said, "Pshaw, my wife ain't got a thing in the world to worry about. I ain't going to be gone but a week and I left her with a side of bacon and a sack of cornmeal."

It is estimated that Virginia's fox hunters spend over $25 million annually to maintain hounds and the horses requisite for formal fox hunting. The same motivation that has prompted this tremendous investment in the sport of the hunt is the motivation that all fox hunters have today for preserving the most important element of fox hunting, the fox himself. It is for this reason that we, the fox hunters, give unlimited support to the program of vaccinating the fox. This is a positive approach that we as men of medicine interested in the health of men and animals now have the opportunity to support, because of the research accomplishments of those of you who have contributed to this Symposium and your like-minded fellow workers. Fox vaccination is a positive approach to the problem of rabies that we fox hunters enthusiastically support.

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Sylvatic Rabies as an Agricultural Problem

Ernest E. Saulmon, D.V.M.[1]

The threat of rabies hangs over the agricultural community like the proverbial sword of Damocles. Each episode is accompanied by its share of personal tragedy and loss, and hysteria out of all proportion to the situation. Fear of a horrible death provides the motivation. The risk of paralysis during administered prophylaxis, following exposure, has also had its sobering effect. In 1959 it was stated that more humans had died from reactions to rabies vaccine than there had been reported cases of rabies (13). Fortunately, recent advances in rabies prevention in the human family have alleviated, to some extent, the risks which were once involved 26, 18, but sylvatic rabies continues to be a grave threat to agriculture.

Rabies has a profound effect on local agricultural communities during an outbreak. Youngsters are encouraged to carry satisfactory weapons to fend off attacks by rabid wild animals, and farmers have been known to go about their daily tasks armed with shotguns. Rural schools have adjusted their schedules so that children will not have to be out prior to daybreak during a winter-time outbreak. There have been many stories of narrow escapes, including the time when an alert schoolbus driver slammed the bus door shut in the face of a rabid fox that was trying to follow children aboard (3).

When the rabies warning goes out, practicing veterinarians are sometimes hard put to keep up with requests for vaccination of cattle and other farm animals.

To make matters worse, rabies education is constantly lagging, particularly among young children, so that they frequently take unnecessary chances with wild animals which suddenly become "tame." The natural curiosity of children cannot be thwarted to the extent that they will cease to poke at a dying fox with a stick or try to pick up a bat that is too sick to fly.

Rabies in the United States was once a predominately urban problem, related to dogs and cats, with infection spreading to humans from this source, but public-health-services sponsored vaccination campaigns have largely controlled urban rabies. The problem is now centered in the rural community, fostered by infection in wild animals.

Headlines in the press continue to scream "Rabies"—1,052 Cases of Animal Rabies in Ontario and Quebec in 1964, in Foxes; New York Records Largest Number of Rabies cases in Northeast, with 92, 45 in Foxes, 28 in Skunks, and 12 in Farm Anima;s Maine had 30 Cases of rabies, 20 of them in Foxes; 7 Cases of Rabies in Vermont in 1964; West Virginia Man Dies of Rabies, Fox Believed Source (14); Minnesota Lad Dies of Rabies, Bit by Skunk while Sleeping in Tent" (12)—and so it goes.

Almost all states have a continuing rabies problem. Perhaps that of Iowa is representative, as reported by Dr. John B. Herrick, extension veterinarian at Iowa State University (6). The number of laboratory confirmed cases in 1965 was 232, down from 463 in 1964. Skunks accounted for the most—118. There were 56 cases in cattle, indicating that the cattle were possibly infected by the rabid skunks. Dogs and cats were the next most frequently infected, and there were six cases in bats. Dr. Herrick stressed that proper compliance with the rabies law and caution on the part of all citizens could reduce the incidence in 1966. He stated that skunks are the biggest problem in control of the disease in Iowa, because there is a great deal of variation in the disease manifestations in this species. "The solution of rabies control in skunks is not easy," Dr. Herrick said. "Who wants to immunize the skunk population?"

Sylvatic rabies is not only a menace to American agriculture; Europe and other continents are having their problems, too. In Europe, a rabies epidemic, blamed mainly on foxes, has crossed the Rhine from eastern Europe and threatens to cover the continent. The number of reported cases of rabies in wild and domestic animals doubled in the past 10 years. The epizootic began near Danzig, Poland, in 1946, and now threatens the Low Countries on the North Sea, while another wave is moving toward Switzerland (16).

In the United States, recent trends in the incidence of rabies in the various species of animals continue, in that the disease is decreasing

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in dogs and cats, but increasing in large farm animals. It is probable that a part of the increase apparent in farm animals is the result of improved diagnostic efforts and techniques. During fiscal year 1965 the number of confirmed cases in cattle reported to the USDA was 769, up from approximately 500 in years prior to 1964. On the other hand, there were only 431 confirmed cases in dogs and cats, considerably fewer than in the past. Skunks continue about the same, while foxes show an increase over rates for the past 7 years. Cases in bats seem to have leveled off after a number of years of constant increase while we were becoming more aware of the disease in this species. It has been estimated that the laboratory confirmed cases represent less than 10 percent of the actual incidence in wild animals (3).

Diagnosis and Clinical Signs. The clinical diagnosis of rabies is one of the most difficult and important diagnoses that a veterinarian is ever called upon to make. The most consistent characteristic of rabies is the extreme variation in the length of the incubation period. For instance, in cattle the period may extend from a matter of days to many months. In one calf it appeared at 10 days of age; infection was thought to have come from the bite of a rabid skunk at time of birth or shortly thereafter (15).

It has often been stressed that rabies in cattle is exceedingly difficult to diagnose clinically. Quick and accurate diagnoses are needed, particularly when there has been human exposure, but sometimes a suspected case lingers on with clinical signs only partially characteristic of rabies (24). As many as nine persons have been reported to have taken courses of rabies vaccine following exposure to a single rabid cow (5).

The majority of rabid cattle die 4 to 7 days after onset of clinical signs, but some may live as long as 14 (23). No one sign can be considered pathognomonic for rabies, and the common symptoms will vary in degree in different cases (24). All central nervous system disturbances in animals must be suspected of being rabies until proved otherwise. Rabies should not be ruled out, even in the case of animals found dead in the field, unless herds are closely observed at daily intervals. Death from rabies has often occurred in cattle, for instance, less than 24 hours after an owner has first noticed that something was wrong.

The major clinical manifestations of rabies in cattle are dullness, inactivity, purposeless walking, yawning, increased salivation, and bellowing, followed by an ascending paralysis with incoordination of the hind legs, stumbling, staggering, and eventual recumbency. In the furious form, mania, wild-eyed expression, loud bellowing, and severe tenesmus are seen early. Inconstant signs are twitching of a local area, particularly the muzzle and face, subnormal temperature, and depressed heart rate. Variations from the usual signs sometimes include normal anal reflex until just before death, incomplete paralysis, and continued ability to eat and drink until the terminal stages of the disease. All cases of paralysis leading to recumbency in cattle, suspected of being neurogenic in origin, should be handled as rabies until proved otherwise.

Bellowing may bring an initial diagnosis of estrus, but that can soon be settled by the bull. On the other hand, if artificial insemination is used, a rabid animal might well be confined for breeding before a true diagnosis can be made. An alert inseminator may be able to tell the difference between rabies and normal estrus, but others probably could not. Closer observation will usually reveal the beginning signs of central nervous system disturbances with progressive incoordination. At this point, differential diagnosis must take into consideration the encephalitides, including listeriosis, the almost endless list of organic and inorganic toxins, as well as certain deficiency diseases and disturbances in metabolism. Injuries to the spinal cord and progressive paralytic diseases must also be considered. Unfortunately, it is not within the scope of this paper to provide overall guidance in differential diagnosis; much education is needed in this field.

A case of rabies in a Hereford heifer in Oklahoma was recently described (17). The animal when first seen had a body temperature of 104°F, and was chewing and salivating with heavy foaming at the mouth. As the disease progressed, there was complete avoidance of food and water. A malodorous watery diarrhea lessened in intensity after dextrose was given. (Although rabid animals usually strain frequently as if to defecate or urinate, diarrhea is not often seen.) The animal's general condition seemed to improve over a period of several days under forced feeding. Although the animal would not drink voluntarily, it constantly stood by the water tank. When its head was forced into the water, swallowing movements could be seen over the esophagus. Later the animal attempted to drink, often immersing its head up to the eyes, but seemed unable to swallow. It would lick a stream of dripping water almost continuously. Bellowing was not reported. Nine days after the animal was first presented for treatment, it went into convulsions, lay on its side, made weak running motions, and died about 4 hours later. Although the brain was negative for Negri bodies, a fluorescent antibody test was positive. The owner was given a course of vaccine injections as a precaution.

Search for a probably persisting rabies reservoir in wildlife is taking much of our attention these days. An inapparent reservoir might explain the persistence of the disease in enzootic areas, or the reappearance of rabies in areas where it had seemed to die out (19). If the disease is always fatal, as has been believed, the natural tendency would be to destroy itself through the elimination of all susceptible animals. Populations of wild animals would be expected to die off to a level at which transmission potential would be nil. However, this does not happen. True, the population is often reduced considerably, but repopulation soon takes place as the wave of the disease sweeps on. Deliberate physical or chemical depopulation of wildlife populations to levels below the potential threshold will stop the spread of rabies in species such as foxes and skunks (9), but relief is usually only temporary.

Research is now underway to evaluate the theory held by a number of scientists that animals and humans may recover spontaneously if nerve tissue is not extensively involved (8). Certainly the fact that bats do not die in wholesale numbers, even when infesting caves in which experimental animals of other species contract the disease without having been bitten, would indicate that these animals have a high degree of natural resistance. If spontaneous recovery does take place, it becomes very important to find out if such animals shed the virus in infectious concentrations during the course of the disease and following recovery. The bat rabies situation is serious; at least five human rabies deaths in the United States have been attributed to attacks by rabid bats (9). The U.S. rabid bat problem may be a "spillover" from the known rabies reservoir among vampire bats in Mexico (21). Migration patterns of U. S. bats permit mixing from time to time.

As part of a search for a potential rabies reservoir in southern New England bats recently, many little brown and big brown bats were captured. Most of them were banded and released in migration studies, but 520 were forwarded alive to the Institute of Laboratories in Boston for rabies examinations. None had been associated with biting incidents. Brain tissues were examined by the usual three techniques—search for Negri bodies, fluorescent antibody staining, and intracerebral mouse inoculation. Rabies virus was demonstrated in eight of the bats, only three of which showed any evidence of abnormal behavior prior to sacrifice at the laboratory (11).

A considerable portion of the rabies problem remaining in dogs in the United States is found along the Mexican Border, presumably brought in from Mexico by stray dogs and wild animals. Animal-tight fences might do much to alleviate the situation, but the last effort to begin to build such a fence is not yet out of the House Committee on Interstate and Foreign Commerce (25).

Large domestic animals also bring in the disease from Mexico from time to time. In December 1964, 912 feeder cattle from Mexico were placed in a feed lot in Arizona. Twelve days later, cattle began to die. When a fourth became ill with the same general clinical signs, a practicing veterinarian was finally called. He suspected rabies, and a laboratory confirmed the diagnosis. In all, nine cattle died with similar symptoms, although only one received laboratory confirmation. The deaths extended over a period of 3 months. It was learned that most of the steers originated in a region of Mexico where vampire bat rabies was quite troublesome at the time. There were no other reports of rabies in any species of animal in the vicinity of the feedlot during the period (4).

Recently a study was made in Tennessee of the incidence of rabies in dogs as compared with foxes (10). Until 1956, the number of cases in dogs exceeded the number in foxes. Since that time more foxes than dogs have had rabies. The decrease of rabies in dogs was attributed directly to the 1951 Tennessee law which made it a misdemeanor to own or harbor an unvaccinated dog. The law also established the Rabies Control Service in the Tennessee Department of Public Health.

Considering only sylvatic rabies, foxes had the most cases among wild animals. Between July 1961 and December 1964, laboratories confirmed 23 cases in bats in Tennessee. To determine the relationship between rabies in foxes and in cave-dwelling bats, an extensive investigation was begun. Cave-dwelling bats are restricted almost exclusively to the middle and eastern sections of Tennessee, where more than 98 percent of the caves are located. Although bat rabies has been reported from western Tennessee at about the same rate as eastern, there seemed to be significantly greater numbers of cases in foxes in the counties with many caves; in fact, the correlation was almost direct. There were 15 counties with 15 or more caves (16 percent of the counties in the state), and these had 33.8 percent of the reported cases of rabies in foxes from 1946 to 1961. Moreover, in 1964, 405 rabid foxes were reported, and all of them were from cavernous middle and eastern Tennessee. Tennessee plans further work to establish the relationship of rabies cases in foxes to caves, with and without bats, fox movements within caves, and bats as food for foxes (10).

Much has been done recently in rabies vaccine production. There are seven vaccines for animals, each one of which has a particular advantage when used in its proper place, but all have definite limitations. Unless a veterinarian is constantly administering vaccines to all species, it will be difficult for him to keep them straight in his memory. On a number of occasions this problem had lead to the death of animals when the wrong vaccine was used. This happens particularly when the modified live-virus rabies vaccine, chick embryo origin, low egg passage, is given to cattle or wild animals such as raccoons and skunks (7).

As long as rabies exists, it will be necessary to maintain a continuing educational program among all veterinarians and medical doctors to assure the use of the most effective vaccine under all circumstances. This, in itself, is a formidable job, but it in no way compares with the enormous task of continually educating the rural populace as to the hazards of sylvatic rabies and the need for vaccine, not to mention the impossibility of adequately informing the urban population prior to its infrequent casual contacts with rural and sylvan environments.

The following types of rabies vaccines for animals are available, with the recommended use indicated:

1. Phenolized rabies vaccine, caprine origin—for horses and wild animals.
2. Phenolized rabies vaccine, ovine origin—for horses and wild animals.
3. Tissue culture rabies vaccine, chemically inactivated—for all domestic animals.
4. Tissue culture rabies vaccine, modified live virus, lyophilized, of low egg passage virus—for dogs.
5. Modified live-virus rabies vaccine, chick embryo origin, low egg passage—for dogs.
6. Modified live-virus rabies vaccine, chick embryo origin, high egg passage—for cats, cattle, and wild animals.
7. Flury modified live-virus rabies vaccine, chick embryo origin, high egg passage—for cats.

Types 1 and 2 provide satisfactory protection for up to a year, but have the disadvantage of short duration of immunity when compared to modified live-virus vaccines. Also, some animals are reported to react to the vaccine by developing irreversible neurological signs.

Type 3, although at present believed to be effective only for a year, may produce a longer span of immunity. The purity of this vaccine, as compared to types 1 and 2, has almost completely eliminated undesirable side effects.

Type 4 is relatively new, and annual revaccination is currently being recommended. Duration-of-immunity studies may extend the period, making it more competitive with other modified live-virus vaccines.

Type 5 is restricted to dogs and is currently the vaccine of choice for this species because it has been demonstrated to confer immunity for at least 3 years. Other than the occasional anaphylactic or allergic reactions to be expected from any injected substance containing foreign protein, unfavorable reactions to type 5 are probably nonexistent. However, reports are occasionally received that cattle and other animals vaccinated with type 5 have died. It is very important that the attending veterinarian frequently review the manufacturers' instructions and use only the proper vaccine for the various species.

Type 6 is the vaccine of choice for cattle and is also recommended for cats.

Type 7 is a relatively new product, recommended for cats 5 months of age and over. The duration of immunity is still under investigation. If it proves effective for more than 1 year, it may have wide acceptance.

Although there are seven types of vaccine now available and licensed, many new products are expected in the near future. Each will have as the ideal goal total protection for the lifetime of the vaccinated individual with no undesirable side effects. Who knows—if a vaccine becomes available giving lifetime protection with a single dose, we may find some volunteers for the job mentioned by Dr. Herrick—"who wants to immunize the skunk population?" (6)

No antibiotic or chemotherapeutic agent has yet been found which is effective against rabies virus. However, immediate treatment of the wound can make the difference between life and death in many instances. If the virus is driven deep into the wound, a cotton swab, rotated in the wound, apparently removes much of the virus, even hours after exposure. First-aid treatment in animals and humans includes permitting the wound to bleed freely, then scrubbing and flushing with any available liquid. In animal studies, when a virus-infected wound was cleaned with tap water, only 5.3 percent of the test animals contracted the disease, even when no further treatment was given. Controls had a mortality rate of 90 percent. Better results were obtained with a 20 percent soap solution and a one percent aqueous solution of benzalkonium chloride (3).

Although these procedures seem quite effective, the World Health Organization Expert Committee on Rabies, as late as 1960, recommended supplemental treatment by the "judicious use of concentrated nitric acid in puncture wounds where the site permits (9)." In those patients that also receive serum, part of the dose should be infiltrated into the tissue beneath the wound, when possible.

In spite of the almost Herculean efforts to provide adequate education to the public, we are often appalled by the lack of understanding of rabies, even among veterinarians. For instance, a recent news story heading read, "Fox Tangles with Farmer and His Cats (2)." The story told of a fox's following a farmer into his barn and attacking some cats and a cow. The fox left when the farmer went to the house for a gun, after he had failed to kill it with a pitchfork.

But here is the clincher that hurts—the article went on to say, "The farmer, members of the Animal Rescue League, and a veterinarian all thought the fox was probably just hungry and not rabid."

When will the veterinary profession fully awaken to its responsibility where rabies is concerned? Surely this is one disease where we must continue to cry, "Wolf!" (or fox, or skunk, as the case may be) until rabies has been wiped from the face of the earth. Exposed persons and animals are our responsibility.

A number of agencies—among them the Food and Agriculture Organization of the United Nations—are recommending that nonvaccinated dogs and cats be destroyed immediately if they are known to have been bitten by a rabid animal (1). If an owner refuses to destroy his animal, confinement in quarantine is recommended for at least 6 months. There is no way to assess the degree of success this approach is enjoying, but the probability is—not much. What owner would willingly part with a pet under such circumstances? Chances are that most control programs will continue to deal only with active or suspected cases, and the information disclosed in the epidemiology that goes with them. Owners of previously vaccinated animals whose vaccinations should still be effective are advised to have them vaccinated again, immediately, and held in confinement or on leash for 30 days.

The destruction of any large domestic animal that has been bitten by a known rabid animal will cause an economic hardship. At first glance, the destruction of a cow which has been bitten seems uncalled for. However, it has been reported that rabies has been contracted by humans who drank the milk of rabid animals when there were open lesions in the digestive tract. Therefore, the destruction of dairy cows seems medically justifiable.

Rabies in wildlife poses a very real and continuing hazard to farm and other domestic animals and the human population. With widespread vaccination of dogs, particularly, and of cats, most cases of rabies in domestic animals mark the end of spread in a chain of exposure. Large domestic animals do not often attack with bites which break the skin, permitting entry of the rabies virus. Such transmission is usually restricted to carnivora or omnivora. Vaccination of all dogs and cats on a continuing basis is fully justified from a public health standpoint. Keeping more than 40 million dogs and cats fully protected in the United States at all times constitutes a substantial drain on the economy, but without a fully protected animal pet population, the threat of rabies in the human family would mount quickly.

Vaccination of 107 million cattle to prevent less than a thousand cases each year is not economically practical. Also, it would not contribute much toward elimination of rabies, because this disease in cattle is almost always a dead end; cattle are seldom a factor in transmitting the disease. The occasional cases in horses are also in this category. Obviously, also, it would not be feasible nor particularly desirable to vaccinate all swine to protect less than a score each year.

Up to now, wild animal population control has been the major effort in the attempt to stop rabies outbreaks in wildlife (20). Obviously, if the disease could be totally controlled in wildlife, rabies would cease to exist. Eradication is a goal greatly to be desired. Wildlife conservation programs, with deliberate perpetuation of species in which rabies is enzootic, seem diametrically opposed to the best public interest as far as rabies eradication is concerned. Reduction of wild animal populations by either chemical or physical means to the point that rabies transmission ceases brings only temporary relief. With relaxation of effort comes a resurgence of population and increased incidence of rabies as the disease again crosses species lines.

Man is constantly moving toward effective control of his total environment. With this must come control of diseases, particularly those which are compounded in seriousness through increased concentration of populations. Some of the choices he must make will be most difficult, not the least of which will be the means he chooses to eliminate rabies. It can be argued that the rabies problem is infinitesimal compared with some of the problems man is bringing upon himself; for instance, the mass destruction of human and animal life on the nation's highways. However, man has always clung to the principle that human disease is morally unacceptable as long as something can be done about it, no matter how costly the method. At this point, I don't think we are ready to accept the concept of "an irreducible minimum" (22) in human rabies deaths, even though there may be only five or six a year in the United States.

Man has been willing to compromise to a considerable extent, however, where animal diseases are concerned. The most effective animal disease eradication programs to date have been based on simple, solid economics. A rabies control program based solely on economics would fail in its inception. Therefore, officials in human and animal health agencies must work together to master this dread disease. If wholesale destruction or control of wildlife is morally unacceptable, perhaps we can challenge our research virologists and engineers to pool their resources to come up with aerosol vaccines which can be effectively used in caves to immunize entire populations of bats in a single effort. Perhaps a vaccine can be mass-produced for incorporation into wildlife baits with a mechanical method of administration built-in which would be activated during consumption. Surely some such combination of methods will eventually provide the answers we seek; we must not rest until rabies has been eradicated. Sylvatic rabies is a serious, continuing danger to agriculture. It will require the best efforts of science and disease control agencies to solve this problem, and solve it we must.

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SYLVATIC RABIES CONTROL

***Aaron Christensen, M.D.*, Chairman**

The Role of the Bureau of Sport Fisheries and Wildlife in Rabies Control

George S. Rost, M.S.[1]

I appreciate this opportunity to represent the Bureau of Sport Fisheries and Wildlife in discussing its animal control function as it pertains to the suppression of rabies.

In order for you to better understand the changes brought about by a recent reorganization, I would like to briefly recall some of the historical developments of the animal control activity of the bureau.

Many of you may remember that the Biological Survey was the forerunner of the Fish and Wildlife Service. An Act of April 25, 1896, appropriated money to the "... Division of Biological Survey: For biological investigations, including the geographic distribution and migration of animals, birds and plants, and for the promotion of economic ornithology and mammalogy, an investigation of the food habits of North American birds and mammals in relation agriculture, horticulture, and forestry. (1)..."

You may ask, "What does this have to do with rabies control?" Actually, the Biological Survey, acting upon the authority granted in the Act, played a major role in stopping the spread of rabies during the epizootic which began in the Southwest about 1915. The disease spread northward into California. It was believed to have been transmitted by coyotes, wolves, other wildlife, and dogs. It then appeared to move eastward into Nevada and Idaho. The Biological Survey was assigned the task of stopping any further spread of the outbreak. Trappers were hired to reduce populations of the vector animals to prevent them from entering communities and endangering human lives. Although the Pasteur treatment was used by many people exposed to rabies during this period, there were some who would not submit to the treatment, claiming there was no such disease, and several lives were lost.

In 1939, Reorganization Plan No. II (1) transferred the Biological Survey functions from the Department of Agriculture to the Department of Interior. A year later, Reorganization Plan No. III, effective June 30, 1940, combined it with the Bureau of Fisheries in the Fish and Wildlife Service. The animal control function of the Fish and Wildlife Service was then assigned to the Branch of Predator and Rodent Control. The Fish and Wildlife Service is now composed of two bureaus: Commercial Fisheries, and Sport Fisheries and Wildlife.

To give you a clear picture of our bureau's present role in rabies control, I would like to tell you of events during the past two years that have brought about certain changes.

Secretary Udall's Wildlife Management Advisory Board was assigned, by the Department of Interior, to study the animal control activities of the Department and to make recommendations for improvement.

On July 22, 1965, Secretary Udall accepted the report of his advisory board—the so-called, "Leopold Report" (2), named for Prof. A. Starker Leopold of the University of California, Chairman. The report was to serve as a general guide for department policy. The board recommended:

1. appointment of an advisory board on predator and rodent control;
2. re-assessment by the bureau of its goals in predator and rodent activities;
3. development of rigid criteria for determining when and where animal control is needed;
4. a greatly amplified research program;
5. a new name for Predator and Rodent Control;
6. formation of a special "flying squad" to assist in emergency situations; and
7. legal controls over the use of poisons.

The Leopold Report generally recommended a complete re-assessment of the goals, policies, and field operations of the Division of Predator and Rodent Control, with a view to limiting the killing program strictly to cases of proven need, as determined by rigidly prescribed criteria.

The board's recommendation that a new name for the Division of Predator and Rodent Control be found was carried out on July 1, 1965, when it was replaced by the Division of Wildlife

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Services. This was more than a simple change in name. It was the establishment of a new division with added responsibilities intended to improve conditions for other wildlife resources.

The new division has retained responsibility for the animal control activity of the bureau, but in addition will engage in wildlife resource enhancement work and pesticide surveillance and monitoring.

Animal control will be available only upon request and with full approval of the landowner or operator, elected officials, and responsible land and resource managing agencies. However, before any new animal control programs are begun, it will be necessary to determine the possible effect of control techniques on other wildlife, particularly rare and endangered species.

In other words, it is not solely the responsibility or prerogative of this bureau to determine when and where control is necessary. This determination must be made in cooperation with others, relying on their specific competence as plans are made to manage rangeland, to protect human health, and to prevent damage to urban or industrial facilities.

On January 21, 1966, John Gottschalk, Director of the Bureau of Sport Fisheries and Wildlife, on behalf of Secretary Udall, announced the basic elements of a new animal-control policy while addressing the National Woolgrowers Association in Portland, Oregon. (3)

The four major goals of animal control include public health and safety. The proposed policy states that animal control will be undertaken "when it is necessary to control animal-borne diseases, such as plague and rabies and to prevent hazards to safety, including aircraft striking birds."

This goal can be pursued either directly, on an operational basis, when the proper methods can be applied only by skilled professionals, or through a program of technical assistance to land users and commercial operators to assist such people in conducting their own control programs.

The memorandum of understanding between the bureau and the Public Health Service is being reviewed to incorporate the new principles of our animal control policy.

To provide fast, adequate assistance when requested, the bureau has formed "mobile forces" teams, which consist of trained personnel that can be dispatched on short notice to emergency situations.

The bureau recognizes that public health agencies are in a position to determine when a disease in wildlife has reached epidemic proportions and is a threat to public health. In keeping with our decision to place more reliance on health officials, we have discontinued collecting rabies incidence data at the state level and will use the information prepared by the Communicable Disease Center for our use.

Before animal control is conducted as a wildlife management tool on any lands, a written agreement must be obtained from the landowner or administrator. Under such an agreement, this bureau reserves the right to determine the method of control and the extent to which it is to be applied.

Research efforts are being expanded to find more selective, effective, humane, and economic methods of reducing wildlife populations. The bureau is cooperating with CDC in the study designed to establish an immune population of foxes in Virginia as a means of reducing the incidence of rabies.

In summary, the bureau has been involved in rabies control since the early 1900's. The "Leopold Report" called for a re-assessment of the bureau's predator and rodent control policy including cooperation in rabies suppression programs. Its role in the suppression of rabies through animal control is carried out through the Division of Wildlife Services. The new animal control policy of the bureau will recognize all the inter-relationships of wildlife before control is carried out.

More reliance will be placed on land administrators and public officials to determine when animal control is needed to achieve their resource management goal. Impact of animal control programs on rare and endangered species is to be considered. Public health agencies are recognized as the logical segment of government to determine when an animal-borne disease is a threat to public health.

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Incidence of Fox Rabies: An Index of the Effectiveness of Trapping as a Control Method

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Since January 1961, a predator rabies control program has been conducted in Virginia. Seven professional trappers employed by the State Department of Health are assigned to counties upon request from the local governing body. Details of the initiation of the trapping program and its operation during 1961 and 1962 are described in an earlier paper (3). The purpose of this paper is to present some of the results of the 5-year trapping program, to question the validity of the reported incidence of fox rabies as an index of the true incidence, and to offer suggestions for the direction of future efforts to control wildlife rabies.

Until the early 1950's, the major animal host of rabies in Virginia was the dog. Since then, the percentage of laboratory-confirmed cases of fox rabies among all animal heads examined annually has steadily increased. From December 1955 through 1959, 58 percent of all confirmed rabies in the state were in foxes; from 1959 through 1965, 73 percent were in foxes. From January 1956 through December 1965, there were 2,502 cases of animal rabies confirmed in Virginia laboratories; 67 percent were in foxes.

Why is so much fox rabies reported in Virginia? Is reporting more accurate than in other states? Are there more laboratory diagnostic facilities? Is there more rabies in Virginia than the surrounding states? Are there more foxes? Is there some environmental or genetic factor influencing the susceptibility to the disease? Whatever the reasons for the magnitude of the problem, the methods of attacking it since 1961 have been determined, although not dramatically successful.

The initial trapping efforts began in January 1961 and were directed toward seven counties in Virginia: Culpeper, Highland, Lee, Montgomery, Scott, Smyth, and Washington (Figure 1). These seven counties had reported more than one-fourth of the fox cases in the state during each of the 5 years (January 1, 1956, through December 31, 1960) prior to the beginning of the program; and the number of fox cases from these seven counties from January 1, 1957, to December 31, 1960, represented one-third of all of the reported cases of fox rabies in the state during that 4-year period (Figure 2).

Figure 1.—*Map of Virginia showing the seven counties trapped during the first year of the program (1961) and one county (Fauquier) which has never been trapped*

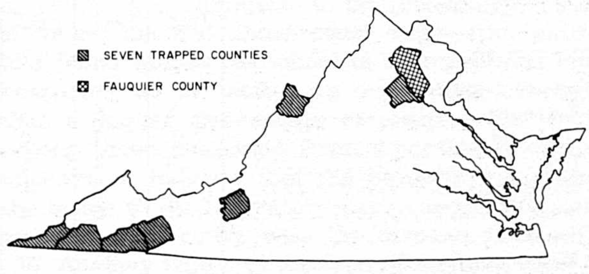
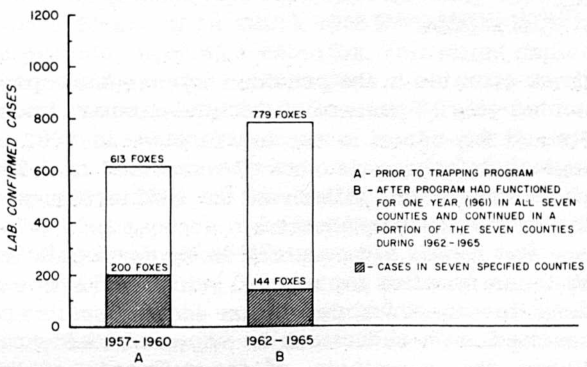


Figure 2.—*Comparison of numbers of laboratory confirmed cases of rabies in foxes in Virginia for two 4-year periods*



In 1961, 247 days were spent trapping in these seven counties (Table 1, column 1961). There were 4,758 predators removed, including 2,470 foxes and 1,400 skunks. It was hoped that extensive predator trapping would result in a reduction in the reported incidence of fox rabies during the next year, and in 1962, the seven counties reported only 10 cases of fox rabies (Table 2, column 1962). This was 47 fewer cases than the average number reported annually by

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Table 1.—*Number of foxes removed and percent of heads positive—8 counties*

County	Foxes removed		Days trapped in each year					Percent positive of all fox heads submitted for examination 1961-1965
	Unborn	Live	1961	1962	1963	1964	1965	
Culpeper	0	396	34	19	0	0	0	46
Highland	36	314	34	0	0	0	0	60
Lee	78	105	33	0	0	0	0	62
Montgomery	447	285	49	13	0	0	0	43
Scott	30	258	24	0	8	0	23	70
Smyth	0	518	30	13	16	6	0	77
Washington	491	433	43	6	24	0	0	79
Fauquier	......	...	0	0	0	0	0	43
Total			247	51	48	1	23	....

Table 2.—*Laboratory confirmed cases of fox rabies in seven "trapped" counties and in one "untrapped" county*

County	Confirmed cases in each year										Foxes removed	
	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	Unborn	Live
Trapped counties:												
Culpeper	3	6	3	1	1	11[1]	4[1]	0	0	0	0	396
Highland	15	3	0	0	0	2[1]	1	0	0	0	36	314
Lee	0	3	6	1	5	32[1]	1	1	0	9	78	105
Montgomery	7	0	4	1	1	12[1]	0[1]	0	3	3	447	285
Scott	1	0	4	19	12	8[1]	0	0[1]	18	29[1]	30	258
Smyth	10	6	12	10	10	11[1]	2[1]	8[1]	7[1]	5	0	518
Washington	6	45	20	15	12	23[1]	2[1]	11[1]	16	24	491	433
Untrapped county:												
Fauquier	1	31	15	3	11	18	2	7	20	17	....	...

[1]County trapped during year.

these counties in the previous 6 years and represented only 10 percent of the total number of confirmed fox cases in the entire state in 1962. A logical inference is that the removal of 4,758 predators in 1961 influenced the 1962 incidence of fox rabies in those counties.

But rabies had occurred in the fox population in these counties for several years, and lowered densities in a fox population seem closely associated with reductions in reported incidence. Hence the magnitude of the influence of the trapping program is impossible to assess. It should be noted that in 1962 the reported incidence of fox rabies throughout the United States was the lowest in 10 years (1), and in one northern Virginia county, Fauquier, which had not been trapped (Figure 1), the decline was almost as dramatic as in the seven trapped counties (Table 2).

In 1962, four of the seven counties (Culpeper, Montgomery, Smyth, and Washington) were retrapped for 51 days (Table 1, column 1962), and 959 predators were removed. This number included 448 foxes. Approximately the same number of foxes were taken from each of the four counties. In 1963, two of these four counties (Culpeper and Montgomery) reported no fox rabies, while the other two (Smyth and Washington) showed an increase in reported fox cases over the previous year (Table 2, column 1963). All four of these counties have approximately the same number of square miles that appear suitable for fox range (2), e.g., non-urban, non-wooded.

During 1963, the two counties (Smyth and Washington) that were reporting an increase in fox cases were being trapped a third time, so some of the increase in positive heads discovered in these two counties during 1963 may have been due to increased interest in reporting, stimulated by the presence of the trappers. The effect of increased interest upon reporting is difficult to assess. Scott County, which was trapped for 8 days in 1963 (Table 1, column 1963), reported no fox cases in that year (Table 2, column 1963). In 1964, Smyth and Washington counties reported about the same number of cases as the previous year; whereas three of the five untrapped counties (Culpeper, Highland, and Lee) showed no increase, one of the counties (Montgomery) showed a slight increase, and the other county (Scott) showed a definite increase in reported cases (Table 2).

By January 1966, more than 33,000 animals had been trapped and killed in 43 of the 47 counties requesting the program. Forty-five percent of these animals were foxes, and 28 percent were skunks. The number of counties reporting wildlife rabies each year remained almost constant from 1955 through 1965, although some new counties appeared occasionally and some previously reporting counties experienced free years.

Since the removal of 33,000 predators has not caused a decrease in the total number of laboratory confirmed cases of fox rabies reported annually from the 43 trapped counties (Figures 3 and 4), their continued rise in reported incidence raises at least one important question: What does the reported incidence of fox rabies from a county really measure? While the number of fox heads submitted for examination appears to give some indication of the density of the fox population, the number confirmed as positive is not a valid

Figure 3.—*Fox rabies reported in the 43 counties trapped at least once since January 1961*

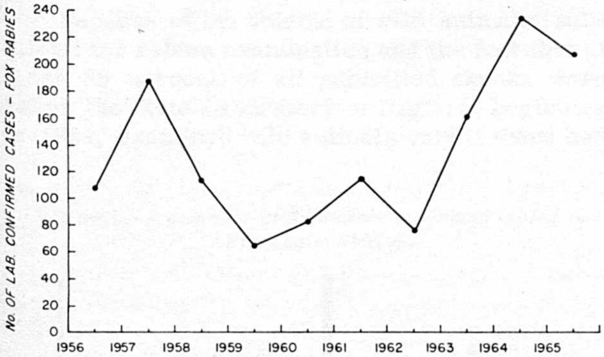
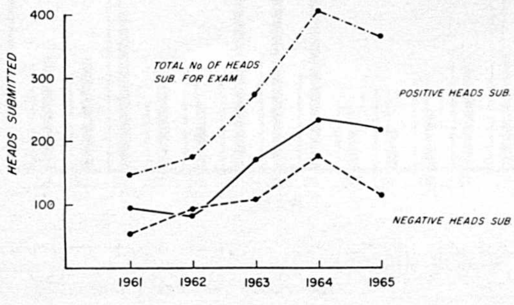


Figure 4.—*Relation of positive fox heads to negative fox heads submitted from 43 trapped counties in Virginia 1961-1965*



index of the true incidence of fox rabies. It is the opinion of the author that the number of positive heads reported by a county during a calendar year primarily reflects local interest in rabies control and is influenced by several factors.

One of these factors is concerned with the activities of local health department personnel. Fox heads are ordinarily taken to a diagnostic laboratory by the local sanitarian. The local health director and sanitarians are therefore able to screen the heads being submitted for examination. There are usually many more negative heads brought to the laboratories from counties where a turnover of health department personnel, i.e., local health directors and sanitarians, has occurred frequently, where local health department personnel seem unfamiliar with the disease for any reason, or where heads are accepted by the health director or sanitarian for laboratory examination in order to establish the existence of the disease in the area. In areas where health department personnel have long dealt with wildlife rabies, few negative heads are examined, probably because only foxes with signs strongly suggestive of rabies are submitted to the laboratory. Thus, if we assume that about equal diagnostic skills are found among personnel in all examining laboratories in the state, we might then conclude that a higher percentage of positive fox heads among those examined from a particular county appears to indicate that the persons submitting the heads to the laboratory have a proportionately greater familiarity with the disease (Table 1).

Another factor is the type of farming done in the area. Dairy cows are particularly sensitive to upsets in their daily routine and, since they are handled twice a day, the owner is likely to notice any evidence of an attack upon the milking herd by a predator such as a rabid fox. This might explain why farmers in communities with dairy herds seem more concerned with wildlife rabies.

An additional influence is the local news media. News concerning animal rabies and human exposures may be handled by the various media with what appears to be indifference or it may be offered in a manner that creates alarm. How such news is presented determines to some extent the local interest in control of the disease, which in turn influences the number of fox heads brought to the laboratory.

Because the reported incidence of rabies may be influenced by such local factors, it has not been possible to measure the effectiveness of trapping and killing predators as a method of wildlife rabies control. Since reporting and local attitudes toward the disease appear so diverse and alterable, the author suggests that future efforts in wildlife control should be aimed at: (1) Reducing the number of susceptible animals by a method more acceptable than killing them; the feasibility of vaccinating wild animal populations in order to reduce the number of susceptibles should be explored. (2) Seeking an explanation for the geographic pattern of fox rabies which is independent of any association with reporting.

There appear to be at least two possibilities that might explain the pattern of this disease: (a) a particular genetic configuration may account for species susceptibility, and that configuration may be clustered, due to inbreeding, in certain fox populations of the world; (b) a latent stage of the virus may exist in large segments of the fox population, spreading to succeeding generations but remaining undetectable by present laboratory means. Several studies (4, 5, 6, 7, 8) support this possibility.

In either possibility, active expression of the rabies syndrome might be triggered by some particular set of environmental circumstances. Neither of these possibilities excludes the continued transmission of the virus through exposure to infected saliva.

Summary: The Virginia Predator Rabies Control Program has operated for 5 years in 43 of 47 counties requesting the service. Although more than 33,000 predators have been trapped and killed, no reduction in the reported incidence of fox rabies beyond the second year of the program has occurred in the trapped counties. The validity of the reported incidence as an index of the true incidence is questioned, since it appears to be strongly influenced by several social factors including reporting and local attitudes toward the disease. For this reason, future efforts at wildlife rabies control might better be directed toward developing other means of reducing the population of susceptibles and toward offering explanations for the present geographic pattern of the disease.

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Rabies and Rabies Control in Wisconsin

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A prerequisite to any consideration of rabies control in Wisconsin is a review of the status of the disease in the state and a resume of some of the factors that have contributed to the situation, followed by a summary of the specific control approaches utilized.

STATUS OF RABIES

The prevalence and relative distribution of rabies in wild and domestic animals in Wisconsin (Fig. 1) are not unlike the prevalence and distribution reported for the United States (1). Despite annual fluctuations in the total number of rabies cases in Wisconsin, the disease in domestic animals has not varied significantly since 1952. The major change has occurred in wild animal rabies, especially the skunk (Mephitis mephitis) (Table 1). In 1958 there were 184 laboratory-confirmed cases of rabies in skunks, more than 10 times the number recorded two years earlier.

Because of the volume of wild animals submitted for rabies examination and the fact that at least 85 percent of all submitted skunks were rabid, the State Laboratory of Hygiene, beginning in 1959, examined wild animals only if there had been human exposure. All of the rabies testing in Wisconsin was conducted by the State Laboratory of Hygiene, Madison. Wild animal rabies figures subsequent to 1959 are therefore not directly comparable with those of prior years. Since this new testing policy came into being, the number of laboratory-confirmed skunk rabies cases, all involving human exposure, has risen steadily, suggesting a recent increase of rabies in this species.

Despite a sizable population, the fox has not been an important rabies victim in Wisconsin (Table 1). Rabies in insectivorous bats was initially detected in Wisconsin in 1957, and since then has been reported annually in low numbers (Table 1). Despite a large and increasing raccoon population, rabies persists in this species at a low level (Table 1).

Until 1960 the principal domestic animal target of rabies was the dog. Since then, the leading domestic animal species has been the cow, closely followed by the dog. Sporadic cases have also occurred in cats, swine, and horses.

Figure 1.—*A summary of laboratory confirmed rabies in Wisconsin, 1952-65*

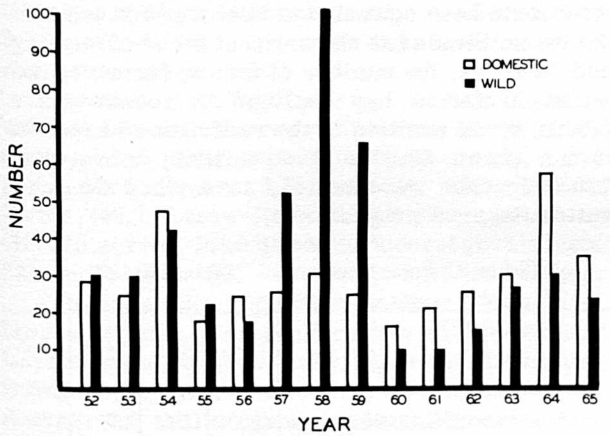

Table 1.—*A summary of animal rabies in Wisconsin 1952-65*

Year	Number of laboratory cases						
	Total	Domestic	Wild	Skunk	Fox	Bat	Raccoon
1952 ..	56	27	29	27	1	0	1
1953 ..	49	21	28	25	2	0	1
1954 ..	90	47	43	36	6	0	1
1955 ..	39	17	22	19	3	0	0
1956 ..	41	23	18	13	2	0	2
1957 ..	74	23	51	37	5	6	2
1958 ..	227	33	194	184	7	3	0
1959[1] .	92	23	69	64	4	1	0
1960 ..	24	15	9	5	1	0	1
1961 ..	30	21	9	5	1	2	0
1962 ..	42	24	18	12	1	5	0
1963 ..	62	33	28	17	7	5	1
1964 ..	95	62	33	12	11	6	3
1965 ..	64	39	25	21	2	1	1

[1]Since 1959, wild animals were tested only if there was human exposure.

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WILDLIFE POPULATIONS

Since the reservoir of rabies in Wisconsin exists among wild populations, a review of some population trends of involved species is appropriate. To census any wild population on a statewide basis is difficult; however, related data can sometimes be utilized to project trends in these wild populations. For example, bounty payment figures provide a kill figure which can be used to project population trends. A summary of fox bounty records (Table 2) suggests a fluctuating population which has steadily increased since 1930. Despite this apparent increase of foxes there has been no conspicuous alteration in rabies prevalence (Table 1). During this 35-year span, fox pelt prices have ranged from $12 to 40¢ with the highest prices paid at either end of the period (2).

Table 2.—*Some wildlife harvest figures in Wisconsin 1920-65*

Year	Species (thousands)		
	Skunk[1]	Fox[2]	Raccoon[1]
1920	56.3	....	4.6
1930	56.7	3.4	6.4
1940	50.7	11.0	13.6
1950	11.6	28.5	34.3
1960	0.8	57.0	50.0
1965	0.4	52.8	63.2

[1]Harvest figures from Wisconsin Conservation Department trapping and hunting records.
[2]Harvest figures from Wisconsin Conservation Department bounty records.

The raccoon is not a bountied animal in Wisconsin, but it is utilized for fur, meat, and sport. Harvest figures for the raccoon (Table 2) have increased from 4,600 to 63,200 in 1965. Raccoon fur prices have varied during this period ($4.35 in 1920; 65¢ in 1948; $2.50 in 1965) and undoubtedly influenced the raccoon harvest. Low fur prices result in less trapping effort and a larger raccoon population. However, since 1945 the raccoon has become an important sports animal, and harvest figures now include a larger proportion of animals taken by hunting than trapping. Increasing harvest figures and reports of crop depredation, vandalism, etc., indicate an increasing raccoon population. This apparent rise in raccoon numbers has not been accompanied by a parallel increase in rabies (Table 1).

The skunk, Wisconsin's major rabies target, was once an important fur animal. In fact it was the second most important fur bearer in the state in 1918, when 74,300 skunks brought Wisconsin trappers almost one-third of a million dollars (3). Because of its fur value the skunk was protected by prescribed trapping seasons until 1930, when the Conservation Commission was asked by the Department of Agriculture to withdraw protection of the skunk since it was a reservoir of rabies. As late as 1945, more than 58,000 skunks were harvested. Fur prices have declined steadily since the mid-1940's and today a prime skunk pelt is worth less than a dollar.

Trapping in general and for skunks in particular has declined rapidly since 1945, and in recent years the number of skunks harvested is less than a thousand. Table 3 reflects this decline in trapping interest despite a marked increase in other outdoor activities. The drop in fur value accompanied by this decline in trapping has resulted in a decreased harvest of skunks and an apparent increase in their numbers.

Table 3.—*Wisconsin Conservation Department license sales 1920-65*

Year	Type of license (thousands)				
	Trapping	Hunting	Deer	Fishing	Sportsman[1]
1920	20.0	(2)	50.2	(2)	(2)
1930	18.9	(2)	77.3	(2)	(2)
1940	15.3	295.7	102.3	233.1	2.8
1950	10.4	455.8	289.4	716.7	20.0
1960	4.4	278.3	269.8	612.9	65.3
1965	2.1	378.8	382.6	490.9	218.5

[1]A sportsman license allows hunting, fishing, and trapping.
[2]Not required.

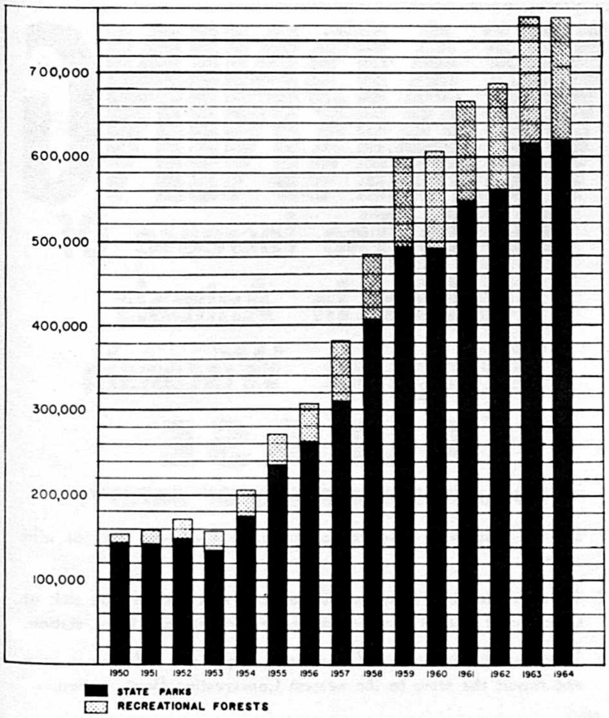
LAND USE CHANGES

There are 36 million acres in Wisconsin, of which 34 percent is crop land and 40 percent is forests. Several important land-use changes in Wisconsin have contributed to changes in wildlife numbers. Similar to the national trend of farming and land use, the number of farms, farmers, and acres in farms has declined in recent years (Table 4). In addition to the reduction of acres in farms (from 23.5 to 21.2 million) more than 770,000 acres were retired in various Conservation Reserve programs (4).

Table 4.—*Farm trends in Wisconsin, 1935-65*

	1935	1945	1955	1965
Total number of farms, thousands	200	178	155	124
Total farm acreage .... millions	23.5	23.7	23.2	21.2
Total land in farms..... percent	66	66	64	60

Figure 2.–*A summary of camper days spent in state parks and forests, 1950-64*



The purchase and development of land for wildlife purposes is a major program in Wisconsin. The Game Division of the Wisconsin Conservation Department in 1927 initiated a land acquisition program. There are 208 individual projects underway or completed in which the Game Division owns 273,000 acres and leases another 291,000 acres for public hunting. In addition there are 4.5 million acres of national, state, or county forest land and private forest croplands available for public recreation. In 1961 the Wisconsin Outdoor Recreation Act established a one cent per pack tax on cigarettes. These funds (approximately 5 million dollars annually) are earmarked for land acquisition to protect and promote natural resources in the state.

Another growing industry in Wisconsin is wildlife farming. There are 27 beaver farms (6,600 acres), 156 deer farms (100,582 acres), 1,012 game bird farms (7,085 acres), 350 muskrat farms (45,717 acres) and 128 shooting preserves (43,775 acres). In addition, the federal government has more than 150,000 acres in wildlife refuges.

Reforestation provides another example of land alteration often conducive to wildlife habitat improvement. In 1959 alone, state nurseries distributed 43 million trees for reforestation (5). Another 1.9 million game food shrubs were sold to private landowners by state nurseries.

Various combinations of the aforementioned changes could have an important impact on wildlife populations, including skunks. Accompanying this increase in the number of potential rabies vectors is the increased opportunity for human contact with wildlife. Wisconsin is in step with the nation in promoting camping. It has 71 state recreation areas with camp sites, 39 federal areas, 169 county or city areas, and 270 private camping establishments (6). In state parks alone during 1964 there were 6 million visitors and over 700,000 camper days spent (Fig. 2).

RABIES CONTROL PROGRAM

Despite these increased opportunities for human contact with rabies, the disease has not been a major human health problem in Wisconsin. There has been one human rabies death, the result of a bat bite, in the state in the last decade.

Although animal bite records are not maintained in Wisconsin, the majority of the animal rabies suspects submitted for diagnosis involve human exposure; therefore, the threat of human rabies is present. To combat this potential rabies problem, various agencies and organizations acting independently and on occasion together have conducted a variety of rabies control programs. Basically the approach has been one of education, involving the public, physicians, veterinarians, and wildlife professionals, as well as pet vaccination programs and the control of local wildlife populations.

The Wisconsin Department of Agriculture through its Animal Health Division promoted an educational program on rabies for Department employees and veterinarians. A monthly computation of animal rabies cases by county was issued to all concerned individuals. The monthly newsletter "Animal Health" supplied free to state veterinarians reported the status of rabies in wild and domestic animals, the location of recent cases, current rules and regulations concerning the disease, and other significant rabies information.

On at least one occasion a geographic section of the state was quarantined because of the threat of rabies.

Local veterinary associations with the aid of University of Wisconsin extension personnel and local officials established county vaccination clinics. Almost half of the 72 counties in Wisconsin sponsored local rabies vaccination clinics which varied in size, procedure, and success. These were local programs, and figures on the total number of pets vaccinated is not available. Most of these programs were initiated in 1958 when rabies was very prevalent in the state. Some programs were discontinued after several years, others exist today, and new clinics are being added annually—especially in recreation areas.

The State Health Department conducted an education program similar to one sponsored by the Department of Agriculture, but directed toward local health agencies and physicians. Data on the status of rabies, appropriate therapeutic procedures, and recommended laboratory protocol were stressed. Their newsletter as well as conventional news media were utilized.

The State Laboratory of Hygiene of the State Health Department conducts all of the diagnostic rabies work in Wisconsin. This is a free service available to all physicians and veterinarians.

Since the major rabies problem involved wildlife, the Wisconsin Conservation Department was concerned and sponsored an active program of information and education. Department personnel were informed on the status of the disease in wild and domestic animals via periodic administrative directives stressing signs of disease, procedure for handling rabies suspects, and the appropriate protocol following human exposure.

Campers were an important high risk group; therefore, an extensive educational program on rabies in wildlife involving the press, television, and radio was directed at this group as well as other outdoor sportsmen. Rabies warnings (Fig. 3) were posted at all state camp grounds and dogs were restrained in all parks. Vaccination of all hunting dogs was promoted.

Local skunk, fox, and raccoon populations adjacent to camp sites were successfully controlled by state trapping personnel. An extension predator trapping program was initiated to teach farmers and other interested sportsmen how to trap wild animals.

The combination of the aforementioned programs was effective in educating the public and involved professionals and in containing this important disease problem in Wisconsin. The continuation of this educational approach with rabies surveillance, vaccination, and control of local wild populations is anticipated and essential.

Summary. Rabies has been present in Wisconsin for many years in both wild and domestic animal populations. Despite annual fluctuations, since 1952 no significant change in the prevalence of rabies in domestic animals has occurred. Wildlife rabies, specifically in the skunk, has varied considerably during this period. Some of the environmental alterations that have contributed to the wildlife rabies picture were new agricultural patterns, reforestation, and increased recreation activities.

Various agencies including the State Departments of Agriculture, Health, and Conservation pursued an informational and educational rabies program aimed at the public, physicians, veterinarians, and wildlife professionals. This in combination with vaccination clinics and control of local wildlife populations appeared to contain the rabies problem in Wisconsin.

Figure 3.—*A typical rabies warning poster utilized at state camp grounds*

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INTERNATIONAL RABIES CONTROL

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Hawaii's Rabies Quarantine System

Ernest H. Willers, D.V.M.[1]

A rabies quarantine system was originally recommended for Hawaii in 1905. That was the year the Division of Animal Industry was created in the Board of Agriculture and Forestry. The board appointed Dr. Victor A. Norgaard, former pathologist with the Federal Bureau of Animal Industry, as the first Territorial Veterinarian and Director of the Division.

Dr. Norgaard's first assignment was to survey the animal health problems in the Islands, and to make recommendations for action programs. In reporting the results of the survey to the board, Dr. Norgaard called attention to the fact that rabies had not yet been introduced into Hawaii and recommended that this fortunate circumstance be protected by establishing a quarantine on imported dogs and cats. The board failed to take action at that time probably because the members did not recognize rabies as a major health problem, having had no experience with the disease.

It was late in 1911 when the need for a rabies quarantine was finally recognized. Dr. Norgaard had been pressing for action since receipt of the Bureau of Animal Industry report for 1909, which contained, an article on "The Nature, Cause and Prevalence of Rabies" by Dr. John R. Mohler. Mohler pointed out that until 1889 rabies was rare in the United States except in Pennsylvania and Massachusetts, and that it was unknown west of the Rockies. In 1900 rabies made its first appearance in Montana, Wyoming, and Colorado, by 1909 it had been diagnosed in all states except Idaho, Utah, Nevada, and Oregon, according to Mohler.

When Norgaard also reported that the state veterinarian of California had declared rabies to be enzootic in Southern California after a series of outbreaks in Pasadena and Los Angeles, the board became alarmed and finally took action. A regulation requiring quarantine of imported dogs and cats to prevent the introduction of rabies was adopted and signed into law by the Governor of Hawaii and became effective March 1, 1912. The duration of quarantine was established in the regulation: "for a period of 120 days, or for such longer period, not to exceed 180 days, counting from the date of embarkation as, in the judgment of the Board shall be necessary." With minor adjustments, that regulation is still in effect. The 180-day maximum restriction was removed in 1940, and the regulation now provides "for a period of 120 days or for such longer period as the state veterinarian shall deem necessary to prevent the introduction of any disease infectious to this class of animals or to man or other animals."

The first regulation applied to dogs and cats "coming from or through any county, state or territory where rabies is known to exist" and required that a permit to import be obtained in advance. By inference, an exception to quarantine was granted animals coming from countries where rabies was not known to exist. In 1926 the wording of the exception was changed to "coming from countries officially declared free from rabies." In place of the import permit an affidavit was required from the captain of the ship stating that the animals had not been allowed ashore at any port en route.

This exception offered some risk even if the integrity of the shipmaster was unimpeachable. Travel to Hawaii by ship from rabies-free countries in Europe would normally involve port calls in infected countries.

For that reason, when the regulation was amended in 1940, exemptions from quarantine were restricted to animals coming under prescribed conditions from Australia and New Zealand. The British Isles were added to the list in 1960 when direct air service was established between London and Honolulu. This new service allowed the animals to make the trip in one aircraft without being transshipped in an infected port.

We would now accept dogs and cats from Norway and Sweden, provided the animals were flown directly to London and thence to Honolulu under the same conditions prescribed for the British Isles. Rabies has not occurred in Norway since 1815, nor in Sweden since 1871, and these countries enforce quarantine restrictions equal to Hawaii's.

When World War II started, we became concerned about the flood of pets military personnel

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might acquire as the campaigns moved across the Pacific. "Experts" told us that we could anticipate an outbreak of rabies or, if it did not occur, we should determine the nature of the peculiar local conditions which prevented this ubiquitous disease from developing in Hawaii. Our experience with troops and pets returning from the Battle of Tarawa dramatically recalled the British experience after World War I, when rabies was reintroduced through Plymouth and spread to seven counties before it could be eradicated. We had to resort to military police power to seize and impound scores of pets, particularly dogs, which had been brought back from the battle areas and smuggled into various rest-camps on three of our islands.

The offenders were Marines. Naval authorities had been less responsive to our request for cooperation in enforcing the quarantine regulation than the commanders of other services. Therefore, conferences were held with representatives of the Medical Department of the Navy, the Army Veterinary Corps, and the local health department to discuss diseases which could be introduced with various classes of animals and birds that might be brought back from the forward areas. The Navy requested that this information be put in writing.

Such a list of diseases was assembled with the assistance of Colonel (later Brigadier General) W. O. Kester, Majors John Cranfield and Roland Scott of the Veterinary Corps, and Dr. A. H. Julien, Inspector in Charge, Bureau of Animal Industry.

When this information was presented to the Navy, their attitude changed to one of full cooperation.

Even so, we were apprehensive of the future when the war's end would bring thousands of troops funneling through Hawaii en route home. We, therefore, decided to take advantage of a section of the original quarantine laws enacted in 1882, authorizing the Minister of the Interior (later the Governor) to prohibit the introduction of animals from any port or country declared by proclamation to be infected.

The information supplied the Navy about the diseases of animals in the war areas was submitted to the Governor of Hawaii with a recommendation that a proclamation be issued prohibiting the introduction of animals, including birds, from all of Asia and Africa, and from all islands in the Pacific and Indian Oceans, except Australia and New Zealand. The proclamation was issued in April 1944 and continued in effect until June 1947. We credit the proclamation in great measure for the desired result that none of the exotic diseases, including rabies, were introduced from the prohibited areas during the latter years of the war and the period of demobilization.

The effectiveness of the quarantine program in Hawaii is established by the fact that rabies has not occurred in the Islands during the 54 years that the system has been in existence. During these years we have processed more than 28,000 dogs, cats, and related carnivores through quarantine without intercepting a single case of rabies. An undetermined number of pets have been abandoned on entry because of the quarantine. Euthanasia was promptly administered to these animals, so we do not know if rabies would have developed if they had been observed for 120 days. On at least one recorded occasion a dog died of rabies en route to Honolulu. This happened abroad a military transport a few days out of Manila. The dog's head was preserved and submitted to the 18th Army Medical Laboratory on Oahu. A positive diagnosis of rabies was made.

We did have a typical case of incipient rabies develop in quarantine in a mature German Shepherd dog in October 1962 (Fig. 1). This dog had been in quarantine about a month when its temperament and disposition changed from friendly-docile to shy and suspicious. It had difficulty drinking water and could swallow large chunks of food only by gulping, due to partial lingual and pharyngeal paralysis. The dog was placed in a security cage for closer observation. During the following 3 weeks, the symptoms gradually subsided. The dog was released at the expiration of the 120-day quarantine period in apparently normal condition (Fig. 2). Two years later the dog died in a local animal hospital following the diagnosis of osteo-sarcoma and surgical removal of a forelimb. At necropsy the diagnosis of osteosarcoma was confirmed, but an astrocytoma was also found in the splenium corporis callosi, adjacent to the hippocampus. In our opinion, this brain tumor, in its early developmental stage, produced the rabies-like syndrome observed in the dog while in quarantine.

The most important aspect of maintaining a rabies quarantine system in a small community like Hawaii is good public relations. We have learned that if you do not have the support of the local citizenry you will soon lose the authority to continue the program. This was dramatically brought home to me in 1934 when, due to the depression and the resulting fiscal economies enacted by the 1933 legislature, both staff and operating budgets were slashed. The level of service in the quarantine station was reduced to such a low point that it adversely affected the health and well-being of the animals. Dogs were dying of malnutrition and fright disease, complicated by a well distributed hookworm infection. The owners were rightfully up in arms. Individual members of the legislature were cornered by the irate owners and persuaded to vote to reduce the quarantine to 30 days or to abolish it entirely

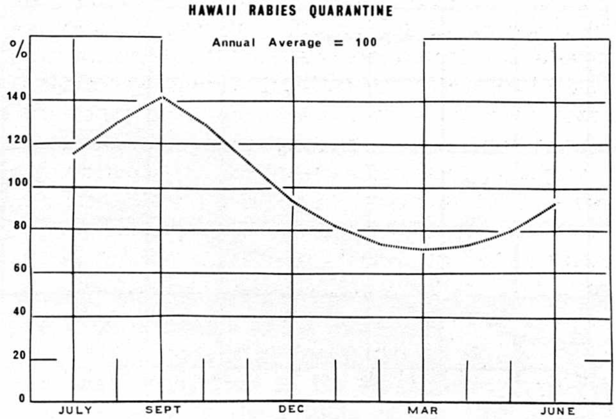
Figure 1.–*Rabies suspect with pharyngeal paralysis one month after entering quarantine*

Figure 2.–*Same dog as Figure 1 at expiration of 120 days quarantine period*

when the next session convened in the spring of 1935. At that point I was asked by the Board of Agriculture to again leave private practice temporarily to take over management of the quarantine operation. I had previously worked on two other special assignments for the board.

It didn't take long to correct the conditions affecting the health of the animals, but the near-hysteria among the owners was a more difficult problem. Fortunately, we received excellent support from the press, the medical profession, and the kennel clubs. But the emotionally aroused owners of animals in quarantine would not pay heed—until they were shown a movie of rabies in a child taken a few hours before death. The film had the desired therapeutic effect and the crisis ended. We have not been confronted with a similar

Figure 3.–*Seasonal index of animal population*



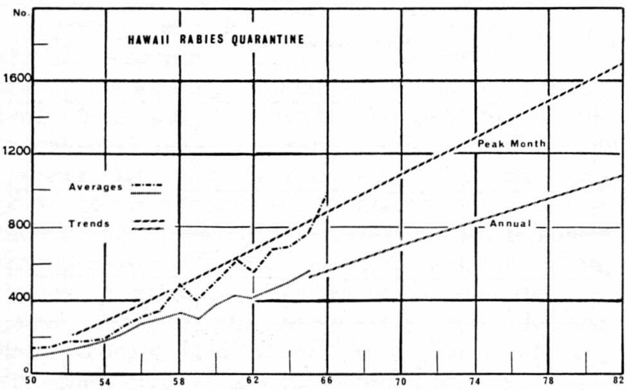
threat to the quarantine system since that incident, but we continue to be aware of the power of public opinion and to frame our policies and operational procedures accordingly.

Our present quarantine station was built on the waterfront, near Honolulu Harbor, during the mid-1920's when more horses and mules than dogs and cats were imported annually. From the beginning of the rabies quarantine in 1912 through 1920, less than 100 pets were processed annually. In the 1920's the number rose to over 200 and then declined to 154 in 1930. During the 1930's the number gradually increased to 360 dogs and 23 cats in fiscal 1940. After a setback during World War II, the numbers increased to a new peak of 513 dogs and 48 cats in fiscal 1950. That number was more than doubled by 1960, when 1,166 dogs and 208 cats were processed. The number has continued to increase during the 1960's until last fiscal year (1965) we handled 1,648 dogs and 361 cats (2,009 total).

We also keep records of the daily animal population from which we calculate monthly and annual averages. The seasonal index of animal population varies from a low of 73 percent of the annual average to a high of 141 percent (Fig. 3). The peak number of pets in quarantine occurs in September following the summertime rotation of military families and the concurrent influx of civilian families. Last September the peak daily population was 985 (808 dogs and 177 cats). A straight line projection indicates that in the early 1980's we can expect an annual average of more than 1,000 dogs and cats and that the peak monthly average will exceed 1,600 (Fig. 4).

From this information it becomes apparent, barring other influences which would alter the trend, that the time will come when quarantine could become prohibitive as a state function because of the tremendous capital investment in land and facilities that will be required. We are, therefore, looking for alternative methods of preventing the introduction of rabies.

Figure 4.—*Projected animal population—1980*



One proposal which, in our opinion, merits investigation is hyperimmunization and measurement of immune response. From the results of some preliminary work with dogs we believe that by administering an antigen intravenously, adjusting the dose to body weight, a high level of immunity can be rapidly induced. We recommend that an experiment be conducted to determine if a critical level of immunity can be induced rapidly enough by this method to consistently overwhelm prior infection as well as protect against subsequent challenge. If such a response could be elicited in a few days rather than weeks or months it would be possible to release the animals from quarantine in a much shorter period of time. This would reduce kennel occupancy per individual animal and allow more pets to be processed each year in the same facilities. Animals that did not develop the specified level of immunity would be held for prolonged quarantine.

I have hope that if this procedure is deemed feasible, a large scale experiment to test the method can be conducted, preferably in a locale where dog and cat rabies is enzootic. I realize that this would be an expensive long-term study.

In the meantime, we are building a new quarantine station in Honolulu. We expanded our facilities to the limit of the 14.5 acres available to us at the present location during the latter 1950's and in 1959 began to search for a relocation site. It was soon learned that state-owned land of suitable size and location was not available, and that private land near the airports and harbors was exorbitantly expensive; the only hope was to acquire a parcel of surplus federal land. The Statehood Act of 1959 directed the military establishments in Hawaii to reappraise their requirements for land and to declare as surplus any found in excess of actual need. After inspecting federal lands on the Island of Oahu which might be declared surplus, a site was selected in Halawa Valley within a radius of 6 miles of Honolulu Harbor, Pearl Harbor, Hickam Field, and the International Airport.

An application for 68 acres of this land, half of which was to be used as a buffer zone, was submitted to the Department of Health, Education, and Welfare in 1962 but was denied for technical reasons. A second application for 32.5 acres was approved with a 70 percent health discount, and transfer of title was completed in October 1964. The first increment of approximately 500 kennels will be ready for occupancy this summer, and the rest of the station will be completed in two additional increments. In addition to the rabies quarantine section, there will be sections for research, for quarantine of other animals, and for the Division of Animal Industry offices and laboratories. Final costs are expected to exceed $3.5 million.

In conclusion and in specific reference to the rabies quarantine system in Hawaii, I want to quote from Dr. Norgaard's report to the Territorial Board of Commissioners of Agriculture and Forestry for 1912, after 9 months' experience with the new quarantine regulation: "The stringent regulation requiring the absolute segregation in quarantine of all dogs (and cats) for 120 days before admission to the Territory, has proven the most annoying problem the Division has had to deal with so far. . . ." We have now had 54 years of experience with the system and I can report to you that the situation has not changed. The pet quarantine is still our most "annoying" problem, but it has kept rabies out of Hawaii.

Rabies in Puerto Rico

Eduardo E. Toro, D.V.M.[1]

The history of rabies in Puerto Rico is rather confused, although the disease was known to exist in the island by the edicts issued since the year 1841, which ordered owners to kill any animals showing symptoms of rabies.

From the years 1910 to 1934, 21 cases of rabies were diagnosed by the Puerto Rico Department of Health and the School of Tropical Medicine.

From 1934 to March 22, 1950, Puerto Rico was considered a Rabies Free Area. On that day, on a small farm in Barrio Monacillos in Rio Piedras, a dog was found with apparent clinical symptoms of rabies. During the next 3 months, 7 cases were diagnosed and confirmed by the laboratories of the Communicable Disease Center and the School of Tropical Medicine.

There are some unanswered questions as to the beginning of the present outbreak. One possibility is that rabies was introduced into Puerto Rico by an apparently normal dog during the incubation period; this dog escaped, bit several animals, including a mongoose, and started the vicious cycle. Another possibility is the role of bat rabies, which has changed many concepts in the epidemiology of rabies.

Dr. Ernest Tierkel, from the Communicable Disease Center, was stationed in Puerto Rico for several months and was the first one to prove the presence of rabies in the mongoose.

This vicious little devil of our animal kingdom was introduced in the West Indies by sugar cane growers in the middle of the 19th century to destroy rats and snakes. The latter is a more possible condition, since there are only a few snakes in Puerto Rico, none of them poisonous.

The mongoose is of no value in controlling the rat population. Their habits are different, the mongoose is a diurnal hunter, the rat is a nocturnal one. Usually the mongoose prefers insects, lizards, toads, poultry, eggs, fish if available, and, if necessary, rats. The mongoose population is calculated at one mongoose per acre, their hunting activities range from one-eighth to one-fourth of a mile and are supposedly migratory in nature.

From the first case of rabies diagnosed in March 1950 to December 1961, 434 cases have been diagnosed in our laboratories. Table I shows the distribution of cases by years and species affected. Two hundred forty-four cases, or 56.2 percent, are in mongooses. Seventy-six, or 17.5 percent, are in bovines. Sixty-four, or 14.5 percent, are in dogs, and the rest are distributed among other species. For some years the incidence in dogs was second to that of the mongoose,

Table 1.–*Animal rabies in Puerto Rico, 1950-65*

Species	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	Total	Percent
Mongoose......	12	41	40	37	21	16	5	8	10	15	21	18	13	11	17	12	297	56
Bovine.........	5	12	10	9	9	3	5	5	2	4	6	6	2	3	2	3	86	17
Canine.........	10	10	8	11	2	4	3	7	3	1	4	1	4	5	7	1	81	15
Equine.........	0	5	4	4	2	2	2	1	1	1	1	1	1	0	2	0	27	5
Feline.........	1	0	1	1	0	0	2	0	0	2	3	2	1	1	4	2	20	40
Porcine........	2	2	2	0	0	1	0	0	1	0	0	0	0	1	0	0	9	2
Caprine........	0	3	0	0	0	0	1	0	0	0	1	1	0	0	1	1	7	1
Total......	30	73	65	62	34	26	18	21	17	24	35	29	21	21	33	18	527	100

[1]Veterinary Section, Division of Preventive Medicine, Department of Health, San Juan, Puerto Rico.

Figure 1.—*Animal rabies in Puerto Rico, 1950-65*

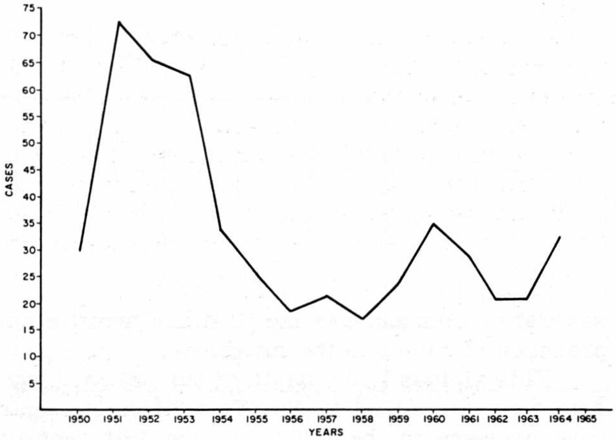
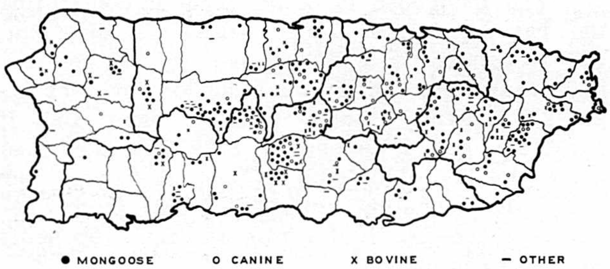


Figure 2.—*Distribution of animal rabies by municipalities Puerto Rico 1950-61*

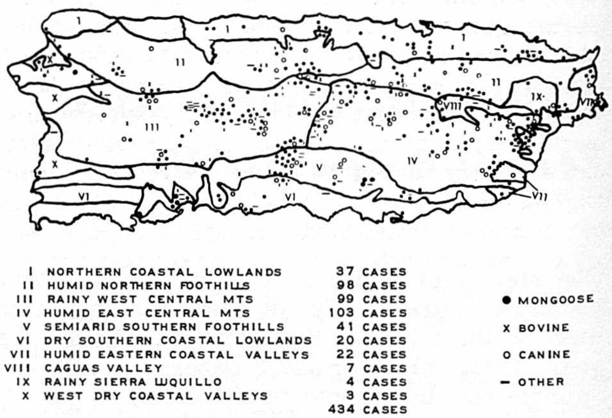


but with the vaccination programs the incidence in dogs is decreasing. Figure 1 shows the number of cases of animal rabies 1950-1965.

For this presentation I have two maps. One (Figure 2) shows the rabies cases by municipalities in Puerto Rico. Each case is located according to the barrios—or wards—in which it was found. This map demonstrates that rabies is concentrated in the central part of the island, although the outbreak started near the metropolitan area of San Juan.

In the second (Figure 3), all 434 cases are placed according to the geographic regions of Puerto Rico. As we observe the map we again note the central location of the cases, in the humid northern foothills, the rainy west central mountains, the humid east central mountains, and the semi-arid southern foothills, where the availability of water, food, shelter, and hiding places is most attractive to the mongoose. Baldwin, Schwartz, and Schwartz, in "The Life History and Economic Status of the Mongoose in Hawaii," state that the mongoose is rarely found in the interior of forest areas. If we observe the geographical map, we notice that in certain areas within this region, where the incidence of rabies has been the highest, no cases have been reported. These are forest areas in the rainy west central mountains, the humid east central mountains, and

Figure 3.—*Distribution of animal rabies according to the geographic regions of Puerto Rico, 1950-61*



rainy sierra luquillo. All these areas are higher than 2,000 feet.

An area to observe in the future is the western part of the dry southern coastal lowlands. This area has been highly irrigated; with the resulting agricultural development, the mongoose may find attractive conditions, and rabies may be reported there in the future.

I was very impressed a few months ago, during a panel discussion on hepatitis in Puerto Rico, by the similarity of the spread of two different viral diseases. The first outbreak of hepatitis occurred in the municipality of Maunabo on the southeast part of the island; then the disease spread into the interior, where it is now firmly entrenched. Similarly the rabies outbreak started in the northeast coast near San Juan and spread into the interior.

Our epidemiologists are calling these areas in the central part of Puerto Rico an island within an island. This concept is bringing intensified efforts in disease control in this island within an island.

Mongoose trapping has been very slow to develop. It is done on a voluntary basis. Recently a private enterprise donated 1,000 traps, and whenever a case is reported, traps are distributed through local civic clubs. These clubs donate additional material for the building of more traps. One project was in the municipality of Coamo early this year. One hundred fifty traps were distributed, and 750 mongooses have been destroyed. Another project was recently started in Utuado, which shows the highest incidence of rabies, with 28 cases. There are no reports available yet. The project has one shortcoming: people get careless with a trapped mongoose, and several persons have had to undergo antirabies treatment because of this carelessness. A mongoose is extremely agile and is very ferocious when trapped. We recommend drowning the animal in the cage.

Usually a normal mongoose tries to stay away from people and animals, but when a mongoose developes rabies, it has a tendency to seek our environment and that of other animals, probably looking for easy access to food and water. Sometimes they even act "cute," sitting in their hind quarters like squirrels. Usually children are the first to notice this strange behavior, and when they seek their newfound friend, the vicious attack takes place. In their search for our environment, they have been found inside homes, barns, warehouses, automobiles, farm machinery, and privies or nearby shrubs.

When a rabid mongoose attacks and takes a firm hold, it usually remains attached to the site of the wound and has to be killed before its hold loosens.

Bovines, the second species affected, are usually attacked while grazing in dense pastures, and the bite is most common in the muzzle and face.

The average rural resident in Puerto Rico owns an average of two dogs. During the daytime they roam the countryside following their owner in his daily chores; thus increasing the chances of coming in contact with a mongoose. When this happens, it is usually a rabid mongoose. It is most difficult for a dog to hunt and kill a normal mongoose. Our vaccination programs are aimed at the rural dog population, which is three times as large as the urban dog population.

Since the outbreak in 1950 no human cases have been reported. The people are well informed about the dangers of rabies and of failure to report attacks. Treatment is usually started within 24 to 48 hours after an attack is reported, but human rabies may be reported any time.

The usual sites of wounds in man are the fingers, hands, and forearms; but attacks on the face, nose, abdomen, and scrotum have been reported.

Bat rabies has not been reported yet. Several incidents involving bats have been reported and laboratory examinations made—with negative results. No extensive studies are planned in the near future to determine if there is rabies in bats. This animal may be playing a very important role in the transmission of rabies not only in Puerto Rico, but in some of our neighboring islands in the Caribbean.

Rabies has been reported in Puerto Rico for the past 12 years, and the mongoose was found to be the reservoir of the disease. No human case has been reported during the present outbreak. The disease is present in the central part of the island where it is most difficult to control, and attempts have been made to eradicate the mongoose, but their population seems to be on the increase. The ever present danger of a human case of rabies points toward increased efforts in the control of rabies in Puerto Rico.

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Rabies in Canada

W. A. Moynihan, D.V.M.[1]

In Canada, rabies is one of the infectious and contagious diseases designated as a "named" disease under the Animal Contagious Diseases Act and Regulations. The diagnosis and control, therefore, are the responsibility of the National Veterinary Services (Health of Animals Branch) of the Federal Department of Agriculture. Under this legislation, broad authority exists for the control of such diseases. In the case of rabies, the application and enforcement of control measures have prevented the disease from becoming established in our dog population and our problem is due to the persistent reservoir of infection in wildlife rather than dog rabies.

The rabies problem in Canada today differs materially from that of earlier years when the disease was centered around the dog. Each outbreak was readily controlled and eradicated. Our problem today relates to the reservoir of infection in wildlife, particularly the skunk and the fox. Fox rabies apparently existed in Canada in the early 1800's, and the death of one of the Queen's representatives, the Duke of Richmond, is attributed to hydrophobia following the bite of a fox. In 1947, significant findings of the disease in Arctic foxes in the North West Territories, Baker Lake, established the fact that there was a reservoir of the disease in our northern wildlife. We are reasonably certain that the disease had existed in the Territories for at least 60 years prior to this date. Shortly after the disease appeared in the northern areas of the Western Provinces, it moved eastward around James Bay and reached epidemic proportions in Ontario in 1957 and 1958.

The major infected area in Canada continues to be Ontario because of the persistent reservoir of infection, particularly in foxes and skunks. There has been some extension into the neighboring province of Quebec. In Manitoba we have a problem with skunk rabies. This outbreak is unrelated to the disease in Eastern Canada and appeared in the absence of any fox problem in that area. From the epidemiology of this outbreak, it would appear the infection came into Canada from the contiguous northern states.

<u>Predator Control</u>. One of the principal requisites for any disease to reach epidemic proportions in wildlife is the existence of a large population of susceptibles. In the infected area in Canada, these conditions have been provided. When rabies breaks out among foxes in a locality having a large fox population, experience has shown that the spread of the disease is likely to continue until the foxes in the area are exterminated. This may take from 1 to 3 years.

An organized wildlife de-population program (sponsored by the Alberta Government) was undertaken in 1953. This involved systematic eradication of wolves and coyotes, using poison baits, snares, and shooting, in a 30-mile zone. These were successful in reducing the wildlife population. It is difficult to evaluate to what degree this contributed to the overall control of rabies. The disease progressed through "buffer zones." Nevertheless, Alberta remained free of the disease from 1958-59 until December 1965.

<u>Control Measures</u>. The National Veterinary Services in Canada provide for prompt investigation and establishment of control measures for this disease. These services are, of course, supported by laboratory diagnostic services. Full-time veterinary officers located at some 130 different field offices across the country are available and trained in controlling infectious contagious diseases such as rabies. Briefly, our control program involves five major points: establishment of a reporting system, prompt investigation of all suspected cases, surveys of wildlife and dog populations, dog control measures, and free dog-vaccination clinics in infected areas.

Once a case of rabies has been confirmed, our veterinary officer establishes a reporting system with all responsible authorities in the area, e.g., medical officer of health, practicing veterinarians, police, and other municipal authorities. All cases in animals are channelled through his office for prompt investigation, and, where necessary, he arranges for diagnostic tests at our federal laboratory.

[1]Associate Director, Contagious Diseases Division, Health of Animals Branch, Canada Department of Agriculture, Ottawa, Canada.

A prompt investigation is undertaken by our veterinarian of all reported suspected cases. Where a person has been bitten or exposed to a suspected rabid animal, the individual is instructed to seek medical advice, and the incident is reported to the local medical officer of health. The decision as to whether or not the person bitten should take rabies treatment rests solely with that person and his medical doctor. In the course of the investigation, our veterinary officer urges the owner of a dog bitten by a rabid fox to destroy it, particularly if there has been no human contact. Any other dogs so exposed or bitten are also destroyed rather than quarantined.

The third step involves a survey of the area to determine the nature of the wildlife population and dog population. In the former case, an estimate is established of the number of foxes and other wildlife in the area. This information is valuable in establishing whether or not there is sufficient wildlife in the area to support an outbreak of rabies.

As dogs may be the means of introducing infection, through contact with rabid foxes, into the dog population of an area, our officer surveys the area to establish whether or not dog-control measures are in operation. Where local municipal authorities are lax in this regard, legislation is available to impose individual or blanket area quarantines.

The fourth step, therefore, is to establish or activate dog-control measures stressing the elimination of unowned or stray dogs. Dog control in our operations is the first line of defense.

In infected areas, the department establishes free rabies vaccination clinics for all dogs and cats. Low egg passage vaccine is provided for use on dogs and high egg passage for cats. Vaccination, however, is considered to be a second line of defense and supplements dog-control measures. In the current year, approximately 85,000 dogs have been vaccinated in Ontario alone. In addition, the department provides vaccine for the vaccination of all dogs in the eastern and western Arctic. Vaccination is undertaken by the Royal Canadian Mounted Police, and all police and native dogs are vaccinated. Two years ago, in addition to rabies vaccine, the department commenced providing distemper and hepatitis vaccine as well. In the Arctic areas, dogs are vital to transportation and survival, and to offset dog disease losses which could be crippling to the natives, this preventive vaccination program was undertaken.

Incidence. The disease has been identified in a wide variety of Canadian wildlife. Approximately 65 percent of reported diagnosed cases involved wildlife, 25 percent domestic animals, and 10 percent dogs. The latter represents a spill-over from the wildlife. Dog rabies is not a problem in any of our large urban centers, and we have experienced little or no cases of the classical dog-to-dog transmission cycle.

The following figures indicate the prevalence and distribution of rabies in Canada.

Human Deaths in Canada due to Rabies
(Bureau of Statistics Figures)

1925	1 (Saskatchewan)
1926	1 (Quebec)
1927	3 (Quebec)
1929	5 (Quebec 4, Ontario 1)
1931	2 (Ontario 1, Alberta 1)
1933	1 (Quebec)
1944	1 (Ontario)
1959	2 (1 man - Peterboro 1 boy - Port Perry)
1960	0
1961	0
1962	0
1964	1 (female: March - Quebec)

The incidence of reported cases of rabies in farm animals is felt to be fairly accurate. In the two provinces where the infection is a problem, Ontario and Quebec, there is a joint arrangement with the federal and provincial governments to pay owners an indemnity for the loss of their animals. This indemnity encourages owners to report their losses and also provides an assistance to them for the loss of their animals.

Bat Rabies. Bat rabies in Canada does not appear to be related to the epizootic or sylvatic rabies which has existed in Canada since 1954. Supporting this view is the fact that 6 cases of bat rabies occurred in southern British Columbia from 1957 to 1960, without other animal species, being involved. There have been no cases of rabies west of the Rocky Mountains since 1955. The main vectors of the outbreak in Canada are foxes and skunks.

Strict control measures have prevented the disease from becoming entrenched in our dog population, and while we in Agriculture are primarily concerned with animal health, rabies insofar as human fatality is concerned, is not a serious matter in Canada.

International Aspects. As part of the responsibilities of our national veterinary service, we see that only healthy animals are exported out of Canada. Consequently, in the event of a diagnosis of rabies on farm premises, the exposed animals are placed under official departmental quarantine for 60 days. This prohibits the movement of any domestic farm animals, particularly cattle, from that farm or for export purposes.

In general, the problem in Canada stems from the reservoir of infection in domestic wildlife; introduction of rabies via imported dogs is not a problem because of our quarantine procedures and regulations applying to dogs entering Canada from the United States and other countries.

For importation purposes, dogs may enter Canada without quarantine from those countries considered free of rabies: Great Britain, Northern Ireland, Eire, Australia, New Zealand, Bermuda, Jamaica, The Netherlands, The Bahamas, Iceland, Denmark, Norway, Sweden, Austria, St. Pierre and Miquelon Islands, and Switzerland.

Dogs from these countries must be accompanied by a certificate from a veterinarian of the national government of the country of origin stating:

(a) that rabies does not exist and has not existed in that country for the 6 months immediately prior to the date of departure;

(b) that to the best of his knowledge and belief the dog has been in that country for the preceding 6 months; and

(c) that the dog has been inspected and found free of any symptoms of contagious disease.

This list of recognized countries is, of course, subject to change as the disease pattern in the world changes.

Dogs from the United States are not subject to quarantine, and their entry is permissible on a rabies vaccination certificate:

"71. (1) A dog may be imported into Canada from the United States at any Customs port of entry if it is accompanied by a certificate signed by a veterinarian licensed in Canada or the United States and certifying that the dog has been vaccinated against rabies during the preceding twelve months; such certificate shall carry a reasonably complete and legible description of the dog and the date of the vaccination of it and shall be initialled by the inspecting official at the Customs port of entry and returned to the owner.

" (2) Subsection (1) does not apply to dogs known as 'seeingeye' dogs or to dogs trained for public entertainment imported into Canada for a temporary stay and kept under direct control while in Canada."

Rabies in Mexico

Jorge Cárdenas Lara, D.V.M.[1]

Operating as a division of the Ministry of Health of Mexico is the Department of Epidemiology and Health Programs. This department has a technical advisory function, providing technical assistance and evaluation from the federal level to programs carried out by the coordinated state health departments throughout the country. Of particular interest to this group is the work being accomplished in vector control, food inspection, and of course, rabies control. This last problem is perhaps a rather new problem, new in the sense that only recently has special attention from the federal level been given to its solution.

There is the problem of lack of resources, and for the conduct of a program such as that involved in rabies control, community support is essential. The organization of the programs designed by the federal health authorities is based on the following: (1) public health education, (2) elimination of street dogs, and (3) massive canine vaccination. This community support for the above program is obtained through PTA groups, joint local rabies committees, service organizations, etc.

In the past, programs carried out in Mexico have been limited because of lack of resources. Four years ago, it was possible to intensify rabies control along the northern border of Mexico, but now that there are prospects of material assistance from the Pan American Sanitary Bureau and United States Public Health Service, we feel that the major obstacle to effective rabies control will have been overcome.

The programs carried out in the past have perhaps been successful to the extent that, generally speaking, there has been a reduction in the number of cases of rabies. This has been accompanied, however, by an increase in the number of people reporting having been bitten. There are other factors about which we are beginning to know something—the possible links between dog-cat-bat-wildlife. In the programs designed for rabies control, the Ministry of Health is involved in only that aspect concerning dogs and cats. The bat and wildlife component of the rabies problem is the responsibility of the Department of Agriculture, with whom close collaboration is maintained.

As far as the problem in dogs is concerned, we in Mexico have a distinct problem. It is estimated that we have over 4 million dogs, of which only a small proportion are vaccinated. As our human population increases, so apparently does our canine population. Thus in Mexico City we now have 6 million people; in Guadalajara, 1.2 million; in Monterey, 1 million. Estimating 1 dog per 10 humans, we have a concurrent canine zoographic explosion going on. Rabies throughout Mexico itself appears to be increasing, even though we are aware that our reporting system is not what it should be. I assume that Dr. Acha in his talk will make mention of the human rabies deaths which have occurred in Mexico. I believe that this figure is well below what the actual status of the disease is.

Nonetheless, within the limits of our past resources, we have done what was possible to reduce the public health hazard. Thus, in Tijuana, recently, we were able to destroy more than 15,000 dogs in a relatively short period, 4 weeks.

At this time, the efforts of the Health Service of Mexico are directed to the development of programs in those areas where the problem is greatest, where local resources permit the realistic mounting of programs, and where veterinarians are available (here I must interject to point out that there are few veterinarians who actively seek public health responsibility). Efforts have been made to ensure that in the veterinary teaching curriculum, the proper degree of importance is given to the zoonoses.

It is with pleasure that I make mention of the collaboration of the Pan American Sanitary Bureau and United States Public Health Service and the Ministry of Health in the program to be carried out in the United States-Mexico Border Area; this program, once realized in the border cities, is scheduled to extend southwards until the whole of Mexico is covered.

During the past few years, between 50,000 and 60,000 dogs have been vaccinated per year in Mexico. Of this, approximately 40,000 dogs are vaccinated annually on the border alone. If

[1]Campana Nacional Contra La Rabia, Mexico D.F., Mexico.

such an effort as this is expended on the 12 cities along the border, consider for a moment the size of the problem that faces us in carrying out similar operations in all the cities of the country. Now that we are assured of not only the interest of the Pan American Sanitary Bureau and CDC, but also their dynamic activity, we feel up to the task. Already for September of this year we have planned a course in FRA technique, to prepare laboratory workers on the border. Two veterinarians are being assigned to the program. The equipment for the program is on order and will soon be available.

I have not made mention of predator control. This actively began with relatively small pilot programs and has now been extended to cover quite large geographical areas. For instance in Sonora last year, a total of 3,890 baits were laid, each bait having about a 7 mile radius of action. Almost the whole state was covered in programs carried out by the Department of Agriculture with the technical assistance of the Ministry of Health and Pan American Sanitary Bureau. In the year ahead, similar programs are planned for Baja California and Chihuahua, extending eastward to the other border states. The rhythm of the work, so ably supported by the Pan American Sanitary Bureau through its public health adviser and CDC, indicates that we are on the threshold of a new and exciting era in rabies control in Mexico. We look forward to demonstrating good results from our efforts.

Discussion--International Rabies Control National Activities in an International Situation

Richard L. Parker, D.V.M. [1]

We have heard from our neighbors that both of the land borders of the United States present rabies control problems. They have suggested that rabies cases may be "exchanged" between the United States and our neighbors to the north and to the south. In such a situation the Public Health Service is the logical agency to spearhead the development of control concepts.

Dog rabies, although representing only a fraction of the total animal rabies problem, is still the greatest source of human rabies infection in this country. Approximately half of all human cases of rabies are exposed by dogs. Almost 30 percent of all U.S. cases of dog rabies are reported from the counties bordering Mexico. This concentration of dog rabies is in part due to the unique problems of this border.

The United States-Mexico Border is nearly 1,600 miles long and is straddled by a dozen or more twin communities. Many of these communities are contiguous. Those of the eastern half of the border are separated by the Rio Grande, a stream which because of irrigation usage has a well regulated flow and is not a major barrier to swimming dogs. Actually, these cities are epidemiologic units which are divided more by administration than geography, and since dogs don't respect man-made boundaries, the problem of control becomes complex.

Since the problem is common to the several states along the border, the Public Health Service has accepted leadership in developing control programs, with coordination facilitated by an international agency, the Pan American Health Organization. Direct assistance is furnished to the local governmental units, through the state health departments, providing stimulation, technical guidance, and coordination of programs with sister communities. The results of this effort can be seen in the new and revised control activities that have developed. Worth mentioning are a new metropolitan city-county program and a general attitude of cooperation on both sides of the border.

The role of a national agency such as the Public Health Service is to supply resources. These resources may be in the form of personnel, as has been the case until now, or may be financial in one manner or another. As has been mentioned, the combined resources of the twin communities are inadequate for effective programs. Ways have been sought and found to overcome this problem. Both national governments will soon combine their resources toward the goal of developing programs that are adequate.

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Discussion--International Rabies Control
Rabies in the Americas

Pedro Acha, D.V.M.[1]

The incidence of reported rabies in animals and man during the years 1954-1965 is shown in Tables 1 and 2 and Figure 1. Although rabies incidence data are not available from every country of the Americas, the disease is thought to be present in each country. A general increase in the number of cases in both animals and man in the Americas has been noted during the past 12 years (Figures 2,3).

A total of 2,407 human rabies cases was reported from the Americas during the 12-year period. The average annual incidence of rabies in humans was 168 cases between 1954 and 1959, while an average annual increase to 233 human

Table 1.–*Reported cases of rabies in animals in the Americas, 1954-65*

Area	Number of cases in animals											
	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965
Total	8,234	7,653	8,041	6,841	7,704	8,286	8,027	8,714	9,849	11,909	13,020	(1)
Argentina	807	1,676	1,217	833	987	(2)	229	1,252	2,314	1,125	2,093	(3)
Bolivia	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(3)
Brazil	(2)	(2)	150	342	334	462	492	[4]223	[4]113	[4]60	[4]162	(3)
Canada	(2)	(2)	180	179	562	904	318	784	1,081	1,137	1,158	1,741
Chile	(2)	(2)	280	197	304	274	605	554	(2)	(2)	218	156
Colombia	(2)	(2)	(2)	(2)	(2)	1,011	839	(2)	(2)	800	(2)	(3)
Costa Rica	0	0	2	39	13	24	172	(2)	6	(2)	(2)	(3)
Cuba	(2)	(2)	(2)	(2)	(2)	340	317	(2)	(2)	71	88	48
Dominican Republic	(2)	6	3	2	4	(2)	(2)	(2)	98	30	34	20
Ecuador	(2)	(2)	(2)	(2)	(2)	(2)	272	155	122	80	68	310
El Salvador	(2)	(2)	31	83	48	97	68	168	206	(2)	72	144
Guatemala	(2)	(2)	67	53	64	117	154	57	157	187	274	187
Haiti	(2)	(2)	2	9	7	(2)	(2)	(2)	(2)	(2)	(2)	(3)
Honduras	(2)	(2)	48	46	44	5	68	154	82	25	58	23
Jamaica	0	0	0	0	0	0	0	0	0	(2)	(2)	0
Mexico	(2)	(2)	(2)	(2)	(2)	65	31	(2)	633	1,874	903	(3)
Nicaragua	65	88	51	52	57	57	48	170	74	75	9	(3)
Panama	(2)	(2)	0	2	2	(2)	(2)	1	1	(2)	3	(3)
Canal Zone	0	0	0	0	0	23	20	2	1	41	(2)	(3)
Paraguay	(2)	(2)	42	75	29	57	28	44	94	57	(2)	(3)
Peru	(2)	(2)	213	300	297	401	553	638	733	1,255	1,424	(3)
Trinidad and Tobago	(2)	58	3	3	11	34	18	(2)	2	2	(2)	(3)
United States	7,328	5,799	5,696	4,546	4,798	4,177	3,567	3,599	3,732	3,929	4,780	4,236
Puerto Rico	34	26	23	23	17	24	34	29	21	21	32	17
Uruguay	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(3)
Venezuela	(2)	(2)	25	11	64	193	181	350	365	1,107	1,644	529
British Guiana	(2)	(2)	8	22	29	(2)	13	500	14	(2)	(2)	(3)
British Honduras	0	0	0	0	0	(2)	(2)	34	(2)	0	(2)	(3)
French Guiana	0	0	0	0	25	4	(2)	0	0	0	0	(3)
Grenada	(2)	(2)	(2)	24	8	17	(2)	(2)	(2)	33	(2)	(3)

[1]Provisional data. [2]Data not available. [3]Disease present. [4]Number of foci or infected herds.

[1]Pan American Health Organization, Washington, D.C.

Table 2.—*Reported cases of rabies in man in the Americas, 1954-65*

Area	Number of cases in man											
	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	[1]1965
Total	165	191	147	163	182	168	154	189	205	304	358	182
Argentina	10	22	16	13	8	20	13	22	[1]40	32	20	19
Bolivia	0	1	0	0	3	9	2	([4])	0	1	0	5
Brazil	20	25	28	33	48	30	9	12	([2])	29	([2])	([2])
Canada	0	0	0	0	0	0	0	0	0	0	1	0
Chile	2	8	4	2	5	6	6	5	9	2	5	1
Colombia	59	52	18	33	23	20	16	45	34	137	195	63
Costa Rica	0	0	0	2	0	0	0	0	0	0	0	0
Cuba	4	1	0	2	4	5	3	1	0	2	0	0
Dominican Republic	0	0	0	0	0	0	1	2	2	1	7	8
Ecuador	([4])	([4])	([4])	([4])	([4])	([4])	18	16	20	16	18	14
El Salvador	1	3	4	2	3	3	3	9	6	4	5	4
Guatemala	5	9	2	4	1	8	10	3	2	2	4	5
Haiti	1	1	0	0	0	0	([4])	1	1	[1]0	[1]0	2
Honduras	([4])	([4])	([4])	1	0	6	0	3	2	3	8	1
Jamaica	0	0	0	0	0	0	0	0	0	0	0	0
Mexico	26	36	31	23	36	30	49	42	54	39	55	33
Nicaragua	([4])	([4])	([4])	3	1	([4])	1	([4])	([4])	1	2	1
Panama	0	0	0	0	0	0	0	0	0	0	[1]0	0
Canal Zone	0	0	0	0	0	0	0	0	0	0	[1]0	0
Paraguay	([4])	3	([4])	2	4	2	0	2	([4])	([4])	0	2
Peru	14	7	15	26	10	8	11	17	11	9	17	7
Trinidad and Tobago	0	0	0	0	0	0	0	([4])	0	([4])	([4])	([4])
United States	15	8	11	6	6	7	2	3	2	1	1	2
Puerto Rico	0	0	0	0	0	0	0	0	0	0	0	0
Uruguay	0	0	0	0	0	0	0	0	0	0	[1]1	0
Venezuela	8	15	18	11	31	14	5	6	21	24	19	15
British Guiana	([3])	([3])	([3])	([3])	([3])	0	5	0	0	0	([3])	0
British Honduras	0	0	0	0	0	0	0	0	0	0	[1]0	0
French Guiana	0	0	0	0	0	([4])	([4])	([4])	([4])	0	0	0
Grenada	([4])	([4])	([4])	([4])	([4])	0	0	0	1	1	([4])	([4])

[1]Provisional data. [2]Cases known to have occurred. [3]Disease not notifiable. [4]Data not available.

cases was recorded between 1960 and 1965. Colombia reported the most cases of human rabies during the past 12 years and a total of rabies in the American between 1954 and 1964 was confirmed by laboratory tests). Mexico and Argentina had the second and third highest incidence of human rabies—454 and 235 cases respectively. Countries reporting one or more human rabies deaths during each year of this 12-year period included Argentina, Colombia, El Salvador, Guatemala, Mexico, Peru, the United States, and Venezuela.

The average annual incidence of animal rabies in the Americas between 1954 and 1964 was 8,981 cases. Dogs accounted for over 90 percent of these animal rabies deaths. The United States recorded more cases of animal rabies than any other country; between 1954 and 1959 most of the cases were in domestic animals, but since 1960 the majority of them have been in wildlife.

Panama, Trinidad, and Jamaica, as well as certain of the other Caribbean islands, have had only wildlife rabies in recent years.

Generally, the increase in animal rabies throughout the entire area has been paralleled by the increase in human rabies. Uruguay reported no animal or human rabies between 1954 and 1963; however, in 1964 a human rabies case was recorded. Between October 1964 and December 1965, there were 153 laboratory confirmed cases of animal rabies, most of them in dogs.

A major problem that is unique for Latin America is the vampire bat, which transmits rabies to cattle and certain other species occasionally. Paralytic rabies in cattle transmitted by bats is prevalent in all countries from Mexico to eastern Argentina with the exception of Peru and Chile (Figure 4). It is estimated that nearly a million cattle die of rabies transmitted by vampire bats in Latin America annually. Al-

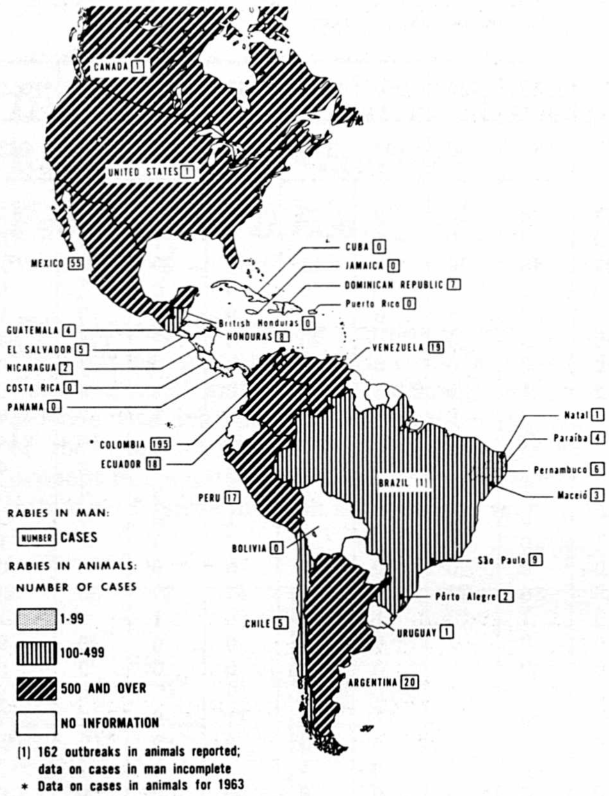

Figure 1.–*Reported cases of rabies in man and animals in the Americas, 1964*

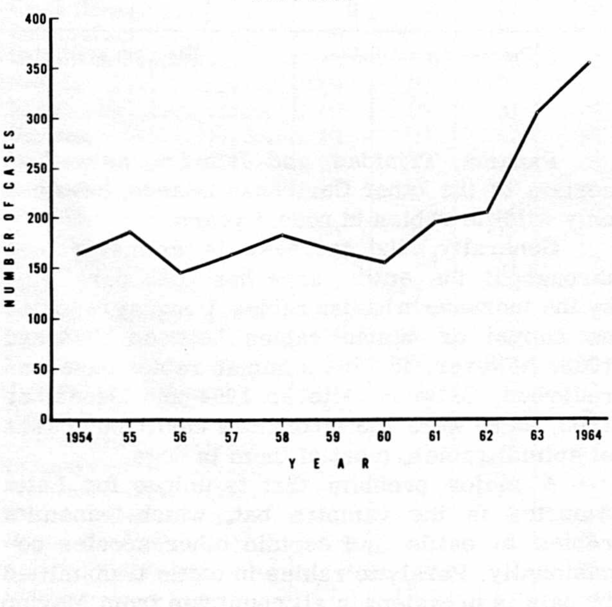

Figure 2.–*Cases of rabies in man in the Americas 1954-1964*

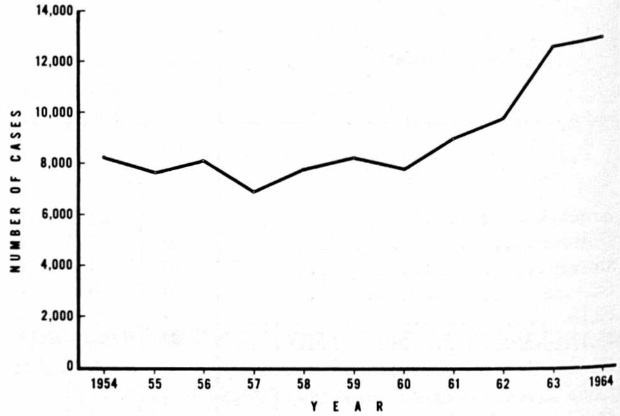

Figure 3.–*Cases of rabies in animals in the Americas 1954-1964*

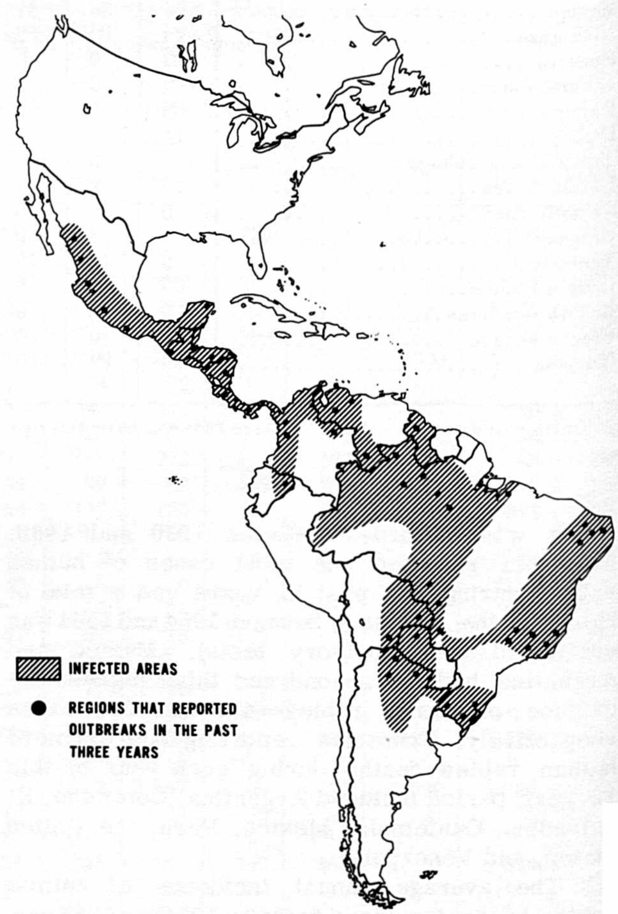

Figure 4.–*Paralytic rabies in cattle transmitted by bats in the Americas, 1965*

Figure 5.–*Rabies in the Americas, 1965*

though three species of hematophagous bats have been reported as positive for rabies in Latin America, Desmodus rotundus is the most frequently infected species.

A map showing the incidence of rabies in the Americas during 1965 is presented in Figure 5.

In Latin America, 42 national laboratories and 11 commercial companies prepare animal rabies vaccines. Both the chick embryo (LEP) and nervous tissue origin vaccines are prepared in 12 of the national laboratories. Four of the national laboratories also prepare antirabies serum.

According to reports of vaccinations of dogs, 10 to 15 percent of the estimated dog population of Latin America is vaccinated against rabies. Most of the stray dog control is effected through poisoning; the intensity of this program varies from country to country.

Throughout Latin America, there is now a better distribution of antirabies treatment biologicals—serum and vaccine—for humans exposed to rabid animals.

Despite more intensive efforts to control rabies in most of the countries of the Americas, the disease has continued to increase generally. Some of this increase is undoubtedly due to improved reporting and laboratory diagnoses. As a result of this increase, more efforts must be placed on control activities throughout the Americas in the future.

Discussion--International Rabies Control
Sociological Problems in a Rabies Control Program in a Community in the Philippines

George W. Beran, D.V.M., Ph.D., and *Samuel B. Gregorio, B.S.*[1]

The success of a canine antirabies program of any magnitude depends upon the organization at the community level (1-3). A vaccination campaign carried out in Dumaguete City, Philippines, in 1964 demonstrated that transmission cycles of rabies can be broken in this region of high endemicity by the development of an adequate immunity level in the dog population. The sociological aspects of planning and carrying out the campaign were found to require much greater effort then the solution to the technical problems. The technical organization of the campaign has been reported (4), and in this communication, emphasis is placed on the sociological setting, drawing illustrative material from the records of the vaccinators.

Dumaguete, a city of approximately 35,000 people, encompasses a rural aggregation of subsistence farmers clustered around a small district of retail shops and home industries in which most shop operators live above or near their places of business. Middle class residential areas are largely occupied by families of teachers, government officials, and some businessmen. These residents, who constituted less than 10 percent of the population of the city, generally responded with civic spirit to the community hazard of canine rabies and cooperated with the vaccinators in the immunization and licensing of their pets.

In the subsistence areas of Dumaguete City, dogs were not maintained as pets within the concept of this term in western countries. In these areas of the city, houses were generally built of light materials and were easily entered by persons from outside the household. Property lines had few demarcations and were criss-crossed by paths leading from principal streets to clusters of residences. Dogs here were valued principally as guards, affording a degree of privacy to the residents. Most of these animals were of nondescript breeding, of medium size, very strong, and quite independent. They lived a partially self-sufficient existence and depended on the owners for only part of their subsistence. Surplus dogs, although usually traceable to an original owner, wandered through the communities searching for anything edible and congregating into packs especially at mating seasons. The relationship of community residents to their dogs is illustrated by the following excerpt from the vaccinators' records. The vaccinators reported that at one house they visited, the owner said, "You see this dog has never in his life been handled and I won't dare touch him [translation from Cebuano]!" Thereupon he feigned interest in having his dog vaccinated. He would allow us to vaccinate but would not lift a finger to help us restrain his dog. We were able to capture the dog with our noose restrainer and we vaccinated it while the owner looked on worriedly."

Most dogs were extremely suspicious of anyone who approached them and would frequently bite anyone, however familiar to the dogs, who attempted to restrain them. Prior to this campaign, community residents considered all dog bites as probable exposures to rabies, and the victims usually were given a prophylactic series of 25 injections of inactivated goat brain tissue antirabies vaccine (5). The fear of dog bites with the attendant discomfort of antirabies prophylaxis added to the dogs' effectiveness as guards and prompted people to avoid disturbing residences or stray dogs. Essentially stray, self-supporting animals were recognized by the community as actually belonging to the household from which they originated. People respected the initial owners' right to reclaim such dogs at any time they wished to care for the animals again. Acceptance of the semi-independent status of community animals and reluctance to antagonize their owners mitigated against the capture or destruction of such dogs. These factors greatly affected the organization of the rabies control program in Dumaguete City. The vaccination campaign was of necessity conducted on a house-to-house basis by teams of vaccinators who captured and injected the dogs with little or no assistance from their owners. Vaccination was the basis of the control program; removal of stray dogs, being much more

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difficult to achieve, was limited to a follow-up effort to remove dogs not recognized by the residents as belonging to the community.

Educational programs that effectively reached middle class residents were accepted but slowly by subsistence farmers and laborers. Although educational media in the forms of outdoor movies on rabies control, public posters, and children's coloring books depicting the story of rabies were prepared in the local dialect and taken throughout the campaign area, acceptance was based more on individual persuasion than on group instruction. Rabies had been endemic in Dumaguete City for as long as anyone could remember, and the people were somewhat adjusted to living with it. People made little mental separation between the frenzied rabid dog that bit without provocation and the guard animal that bit when approached. It was generally considered that exposure to rabies could be avoided by being careful not to molest dogs, and unprovoked animal bites were as frequently attributed to fate as to a diseased condition of the biting animal. The pattern of life in the subsistence areas of the city was highly stabilized and persons who sought change characteristically found it by emigration rather than by effecting internal changes within the social structure. A dog vaccination program brought an additional responsibility into the community with many ramifications, some social and some financial, and people were hesitant about accepting it.

This is illustrated by the following excerpt from the vaccinators' records: "One dog owner claimed that her dog was very friendly and seldom left her house so that it was not necessary for us to vaccinate. We tried hard to convince her but she stood like a rock on her story. The owner of the next house received us well and we thanked her, saying that her acceptance was a noble act to safeguard herself and her neighbors. We recounted the cases in our city in which people had died of rabies following bites from their own dogs. We were about to leave when the woman in the first house called to us. She had been listening to our conversation and was now willing to let us vaccinate her dog."

The financial costs directly or indirectly incurred by dog owners in the rabies control program were a serious problem in the subsistence population, in which the use of limited funds was equated directly with the welfare of the immediate families. These people were extremely hesitant about spending money on their dogs which might only have future rather than immediate benefit to themselves, and about taking community view of their financial responsibility in rabies control. They viewed entrance into this program as involving costs for vaccination and collars for dog licenses, and responsibility for periodically repeating this process, all of which would be commitment to an additional financial burden. This is evidenced in the following excerpt from the vaccinators' records: " 'Imagine,' one woman sighed, 'even the dogs now have to be taxed. Good, if I had the money [Translation from Cebuano].' We explained to her that the P1.50 (approximately U. S. $0.38) charge only covered the cost of the vaccine and not even the time and labor of the vaccinators. We were not getting anywhere when we noticed that she had little children. We told her about a two-year-old child in our city who died of rabies following a bite by the parents' own dog and in spite of having received the regular 25 doses of vaccine. You should have seen the expression on her face as she went to the kitchen for her money while we vaccinated her dog."

Even at the minimum fee charged for the vaccine, only about a 25 percent collection was accomplished, and it was essential that the vaccination of individual dogs not be predicated on payment of the fee. Used plastic venoclysis tubes were obtained from the local Red Cross Blood Bank for use as dog collars, but the need far exceeded the supply. The indigent people of this community were dependent on the government health services for vaccines against smallpox and cholera, and it was difficult to deviate very far from this pattern in the immunization of their dogs against rabies.

Summary. The sociological problems of a community rabies control program in Dumaguete City, Philippines, were greater than the technical problems. The semi-independent existence of dogs in the lower class areas of the city, the ineffectiveness of educational programs at the group level and the reticence of families to spend their limited funds for benefits not immediately felt required carefully planned and extensive efforts at the level of individual households. The completion of a successful dog vaccination campaign in the city provided evidence that rabies control can be achieved in this type of society.

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